Evaluation of Patients with Head and Neck Cancer by Means of $^{99m}$Tc-Glucarate

Juan P. Gambini1, Margarita Nuñez2, Pablo Cabral3, Martín Lafferranderie4, Javier Noble5, Eduardo Corchs5, Ricardo D’Albora4, Eduardo Savió6, Lucía Delgado7, and Omar Alonso1,2

1Nuclear Medicine Center, Clinical Hospital, University of Uruguay, Montevideo, Uruguay; 2School of Medical Technology, Nuclear Medicine Technology Program, University of Uruguay, Montevideo, Uruguay; 3Nuclear Investigations Center, School of Science, University of Uruguay, Montevideo, Uruguay; 4Department of Otorhinolaryngology, Clinical Hospital, University of Uruguay, Montevideo, Uruguay; 5Department of Radiology, Clinical Hospital, University of Uruguay, Montevideo, Uruguay; 6Department of Radiochemistry, School of Chemistry, University of Uruguay, Montevideo, Uruguay; and 7Department of Oncology, Clinical Hospital, University of Uruguay, Montevideo, Uruguay

Preliminary findings have suggested that $^{99m}$Tc-glucarate has tumor-seeking properties. The purpose of this study was to explore the potential of this tracer to evaluate malignant head and neck tumors by means of SPECT/CT software fusion imaging. Methods: Eleven male patients with advanced head and neck carcinoma were included in the study: 9 with locally advanced disease and 2 with clinical suspicion of local relapse. Scanning started 3–6 h after the injection of 1,110 MBq of $^{99m}$Tc-glucarate. Planar and SPECT images of the head, neck, and thorax were acquired. Three-dimensional images were also coregistered with CT. Results: We found $^{99m}$Tc-glucarate uptake in all suspected lesions. SPECT/CT fusion imaging was helpful in all cases for topographically localizing the tracer foci. Conclusion: $^{99m}$Tc-glucarate can be considered a potential tracer for the evaluation of patients with head and neck tumors.

Key Words: head and neck tumors; $^{99m}$Tc-glucarate; SPECT/CT software fusion

DOI: 10.2967/jnmt.109.062927

Although $^{18}$F-FDG PET has set a new standard for the evaluation of cancer patients (1), the development of new $^{99m}$Tc-based SPECT radiopharmaceuticals may become an attractive alternative because of its lower cost and better availability. Glucarate is a 6-carbon dicarboxylic acid, a product of the metabolism of $\alpha$-glucuronic acid that can be labeled with $^{99m}$Tc (2). $^{99m}$Tc-glucarate has been described as an agent avid for acute cerebral injury and myocardial infarction (3–7) and as a possible tumor tracer (8–13). The mechanism involved in uptake of $^{99m}$Tc-glucarate by necrotic cells may be related to binding of the tracer to histones in the cells (14–16). Besides, because of the similarity of $^{99m}$Tc-glucarate to fructose, $^{99m}$Tc-glucarate enters the cell by this metabolically active sugar transport system (8). Furthermore, Ballinger et al. (17) reported that $^{99m}$Tc-glucarate showed a 2- to 3-fold enhanced accumulation in hypoxic cells relative to aerobic cells in an in vitro system of cultured ovary fibroblasts.

Malignant tumors arising in the head and neck constitute a diagnostically challenging pathology representing about 3% of all newly diagnosed cases of cancer in humans (18). The purpose of this study was to explore the potential of $^{99m}$Tc-glucarate to evaluate malignant head and neck tumors by means of SPECT. Additionally, SPECT/CT software fusion was performed to increase diagnostic precision.

MATERIALS AND METHODS

Eleven male patients with advanced head and neck squamous cell carcinoma were included in the study: 9 patients with locally advanced disease enrolled before surgery and 2 patients with clinical suspicion of postsurgical local relapse (Table 1). Imaging was performed at the Clinical Hospital of the University of Uruguay after ethical clearance had been obtained. Before undergoing scintigraphy, all patients had pathologic confirmation of their primary tumors, as well as corresponding conventional imaging examinations. Once written informed consent had been obtained, imaging started 3–6 h after the injection of 1,110 MBq of $^{99m}$Tc-glucarate, with a 10-min planar image of the head, neck, and thorax being obtained in a 256 × 256 matrix. The images were acquired with a digital $\gamma$-camera equipped with a double-head detector (Nuclide Spirit DH-V; Mediso) and low-energy high-resolution collimators and connected in series to a dedicated computer (Mirage; Segami Corp.). The SPECT studies were performed immediately afterward, using a 128 × 128 matrix, 360°, 120 steps, and 30 s per step. Images were reconstructed using the ordered-subsets expectation maximization iterative method and a postreconstruction Butterworth filter of fourth order with a cutoff frequency of 0.25–0.35 Nyquist. Three-dimensional images were also coregistered with CT to better localize the uptake. CT was performed with a dual-slice Twin Flash scanner.
ELSCINT), using a 250-mm scan diameter, 120 kV, 100 mAs/slice, a pitch of 0.7–1, and a $512 \times 512$ matrix. Intravenous contrast material was used in all cases.

Images were fused using the Mutual Information Registration software available on the Mirage workstation (a fully automated registration method that allows volume alignment by mutual information).

SPECT and CT were performed within 2–5 d of each other and with the patients in the same position to decrease misregistration errors. $^{99m}$Tc-glucarate was prepared from current good manufacturing practice glucarate formulation kits (School of Chemistry, University of Uruguay). Radiochemical purity was greater than 90% in all cases.

**RESULTS**

We found $^{99m}$Tc-glucarate uptake in all primary tumors ($n = 9$), in regional lymph node basins ($n = 4$), and in those regions where a local relapse after surgery was suspected ($n = 2$). Furthermore, we did not find significant tracer accumulation in thyroid tissue or in salivary glands. All lesions were confirmed by pathology to have a low to moderate degree of necrosis. Pathologic TNM staging was used to unify pathology findings from different head and neck tumors. Images did not show other areas of abnormal uptake, and there was no clinical or radiologic evidence of distant metastases. SPECT/CT fusion images were of good quality, allowing in all cases good topographic localization of tracer foci (Figs. 1 and 2). Moreover, hybrid images were particularly useful in those patients with imaging findings of local relapse that were further confirmed by pathology after surgery (Fig. 2).

**DISCUSSION**

Our results demonstrate the tumor-avid properties of $^{99m}$Tc-glucarate in patients with malignant head and neck lesions. All primary and local-relapse lesions were detected with good contrast.

On the basis of our prior findings (12,13), $^{99m}$Tc-glucarate could be considered a candidate agent for the detection of malignant lesions in the thorax and in the head and neck. Unlike $^{99m}$Tc-sestamibi, $^{99m}$Tc-glucarate does not accumulate in the thyroid and salivary glands and thus allows images of good signal-to-noise ratio. Moreover, this radiopharmaceutical is not affected by the expression of multidrug resistance–associated protein 1, whereas $^{99m}$Tc-sestamibi accumulation in tumor cell lines is inversely proportional to the expression of the cell multidrug resistance phenotype (10).

The mechanisms involved in such uptake could be related to the high metabolic rate of tumors together with hypoxic, necrotic, or apoptotic processes that could dynamically coexist in different proportions within each malignant lesion. The impact of each possible mechanism may play different roles according to the type of lesion (primary, local relapse, lymph node metastases) and lesion size because tracer sensitivity might be limited for tumors smaller than those included in this series.

SPECT/CT software fusion images were helpful to establish the correct anatomic location of $^{99m}$Tc-glucarate foci. It is well known that SPECT/CT has been used for the evaluation of patients with various malignant tumors with good results (19). The alternative to the more expensive

<table>
<thead>
<tr>
<th>Patient</th>
<th>Primary tumor location</th>
<th>Age (y)</th>
<th>Sex</th>
<th>pN</th>
<th>Stage after surgery of primary tumor</th>
<th>Size (cm)*</th>
<th>Pathology</th>
<th>Regional node involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oropharynx cancer</td>
<td>55</td>
<td>M</td>
<td>N0</td>
<td>IV</td>
<td>5.5</td>
<td>MDEC</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Supraglottic tumor</td>
<td>46</td>
<td>M</td>
<td>N2c</td>
<td>IVA</td>
<td>3.2</td>
<td>MDEC</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Nasopharynx tumor</td>
<td>61</td>
<td>M</td>
<td>N0</td>
<td>IV</td>
<td>4.6</td>
<td>Undifferentiated carcinoma</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>Larynx cancer</td>
<td>62</td>
<td>M</td>
<td>N0</td>
<td>IV</td>
<td>3.8</td>
<td>WDEC</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>Glottic and supraglottic cancer</td>
<td>80</td>
<td>M</td>
<td>N0</td>
<td>III</td>
<td>1.8</td>
<td>WDEC</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>Carcinoma of right retromolar trigone</td>
<td>57</td>
<td>M</td>
<td>N1</td>
<td>IV</td>
<td>6.2</td>
<td>WDEC</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>Tonsil cancer</td>
<td>55</td>
<td>M</td>
<td>N1</td>
<td>IVA</td>
<td>3.8</td>
<td>WDEC</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>Larynx cancer</td>
<td>66</td>
<td>M</td>
<td>N3</td>
<td>IV</td>
<td>3.7</td>
<td>WDEC</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>Right inferior maxillary tumor</td>
<td>67</td>
<td>M</td>
<td>N0</td>
<td>IV</td>
<td>3.9</td>
<td>WDEC</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>Right nasogenian fold tumor (postsurgery)</td>
<td>65</td>
<td>M</td>
<td>Local relapse?</td>
<td>IV</td>
<td>4.8</td>
<td>Sclerosant basocellular epithelioma</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>Oropharynx tumor</td>
<td>50</td>
<td>M</td>
<td>Local relapse?</td>
<td>IVA</td>
<td>2.2</td>
<td>PDEC</td>
<td>+</td>
</tr>
</tbody>
</table>

*Greatest dimension.

MDEC = moderately differentiated epidermoid carcinoma; WDEC = well-differentiated epidermoid carcinoma; PDEC = poorly differentiated epidermoid carcinoma.

**TABLE 1**

Patient Characteristics
hybrid SPECT/CT technology is software fusion of CT with SPECT data. In our series, because of the unique anatomic characteristics of the head and neck region, we obtained fused images of good quality without using external markers. Even though this technique is more time-consuming and may have disadvantages related to misregistration, the patient is exposed to less radiation and the imaging can be performed without significant additional costs.

CONCLUSION

Our preliminary data suggest that $^{99m}$Tc-glucarate can be considered a potential tracer for the evaluation of patients with head and neck tumors. The good tumor-to-background relation of $^{99m}$Tc-glucarate allows fusion imaging with CT. These results must be validated in a larger series of patients with an appropriate follow-up.

ACKNOWLEDGMENT

This work was partially supported by a research grant from the Comisión Sectorial de Investigación Científica (CSIC), University of Uruguay, Montevideo, Uruguay.

REFERENCES


Erratum

Because of a production error, the “Message from the President” in the September issue was incorrectly attributed to the outgoing president, Mark Wallenmeyer, instead of to the incoming president, Cybil J. Nielsen. We regret the error.
Evaluation of Patients with Head and Neck Cancer by Means of $^{99m}$Tc-Glucarate

Juan P. Gambini, Margarita Nuñez, Pablo Cabral, Martín Lafferranderie, Javier Noble, Eduardo Corchs, Ricardo D'Albora, Eduardo Savio, Lucía Delgado and Omar Alonso

Doi: 10.2967/jnmt.109.062927

This article and updated information are available at:
http://tech.snjmjournals.org/content/37/4/229

Information about reproducing figures, tables, or other portions of this article can be found online at:
http://tech.snjmjournals.org/site/misc/permission.xhtml

Information about subscriptions to JNMT can be found at:
http://tech.snjmjournals.org/site/subscriptions/online.xhtml