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

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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

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 D-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 γ-camera equipped with a double-head detector (Nucline 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

TABLE 1
Patient Characteristics

| | | | | | Stage after surgery of | | | ^{99m}Tc glucarate | |
Number	Primary tumor location	Age (y)	Sex	pN	primary tumor	Size (cm)*	Pathology	Primary lesion or local relapse	Regional node involvement
1	Oropharynx cancer	55	M	N0	IV	5.5	MDEC	+	−
2	Supraglottic tumor	46	M	N2c	IVA	3.2	MDEC	+	+
3	Nasopharynx tumor	61	M	N0	IV	4.6	Undifferentiated carcinoma	+	−
4	Larynx cancer	62	M	N0	IV	3.8	WDEC	+	−
5	Glottic and supraglottic cancer	80	M	N0	III	1.8	WDEC	+	−
6	Carcinoma of right retromolar trigone	57	M	N1	IV	6.2	WDEC	+	+
7	Tonsil cancer	55	M	N1	IVA	3.8	WDEC	+	+
8	Larynx cancer	66	M	N3	IV	3.7	WDEC	+	+
9	Right inferior maxillary tumor	67	M	N0	IV	3.9	WDEC	+	−
10	Right nasogenian fold tumor (postsurgery)	65	M	Local relapse?	IV	4.8	Sclerosant basocellular epithelioma	+	−
11	Oropharynx tumor	50	M	Local relapse?	IVA	2.2	PDEC	+	−

*Greatest dimension.

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

(Elscint), using a 250-mm scan diameter, 120 kV, 100 mAs/slice, a pitch of 0.7–1, and a 512 × 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
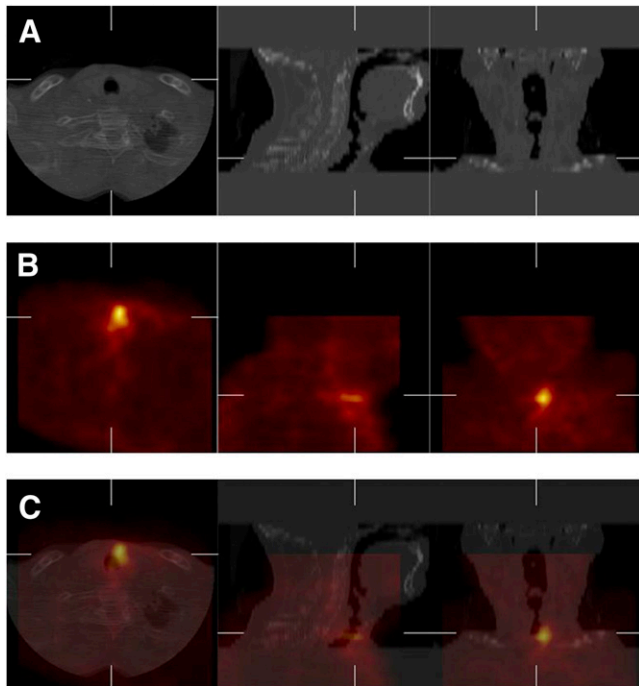
FIGURE 1. A 62-y-old patient with larynx cancer. (A) Head and neck CT image of patient showing transaxial (left), sagittal (middle), and coronal (right) slices. (B) Head and neck ^{99m}Tc-glucarate SPECT image. (C) SPECT/CT fusion image. CT images show thickening of soft tissues of left side of subglottis with eccentricity and luminal stenosis. Fusion images show intense focal uptake in that region.
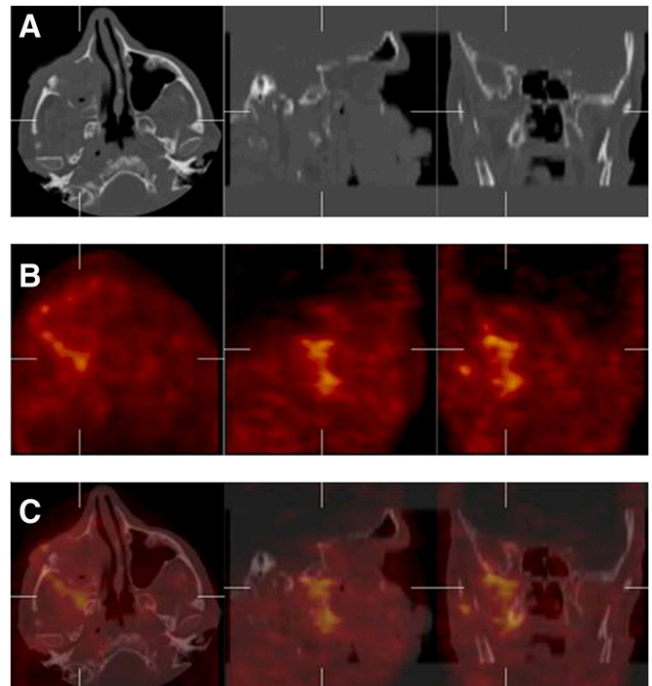

FIGURE 2. A 65-y-old patient with clinical suspicion of local relapse from previously resected sclerosant basocellular epithelioma in right nasogenian fold. Patient underwent right maxillary antrectomy. (A) CT images show surgical sequel at roof of right maxillary sinus with mucosal thickening of cavity. (B and C) ^{99m}Tc-glucarate shows intense uptake (B) that in fusion images corresponded to location of pterigomaxilar fossa (C). Lesion was further confirmed as local relapse by biopsy.

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.

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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.