Speech-Related Visualization of Laryngeal Muscles with Fluorine-18-FDG

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This study describes the physiological uptake of ^{18}F-fluoro-2-deoxyglucose (FDG) by the laryngeal muscles secondary to activation of the patient's vocal folds and related laryngeal muscles during speech. **Methods:** Twenty-four patients undergoing routine PET scans were randomized into two groups to ascertain the relationship between FDG uptake in the laryngeal region and speech. One group was assigned to talk and the other group remained silent during the injection and uptake period of FDG. **Results:** FDG uptake in the laryngeal muscles in the scans was correlated with speech. Patients who spoke continually during the uptake period had high-grade FDG uptake, those who spoke intermittently had low-grade uptake and those who remained silent had no detectable increase in FDG uptake in the region of the larynx. **Conclusion:** The relationship between the degree of laryngeal muscle uptake and speech provides useful information to allow differentiation of physiological from pathological uptake in the neck.

Key Words: fluorine-18-FDG; PET; laryngeal muscles

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PET imaging with the radiolabeled glucose analog, ^{18}F-fluoro-2-deoxyglucose (FDG) is an important tumor imaging modality, particularly for the staging of cancers and in the differentiation of post-therapy changes from residual or recurrent tumors. It is therefore important to accurately define patterns of physiological uptake of FDG to avoid false-positive results which may lead to inappropriate patient management. Although FDG has been widely studied as a PET radiotracer, the literature still suffers from a paucity of data relating to the normal tissue distribution of FDG. Knowledge of this normal distribution is vital to differentiating pathological from physiological tracer uptake.

FDG, as an indicator of local metabolic glucose utilization, localizes in striated muscle (*1*) and contraction-induced increases in FDG uptake by striated muscle have been previously reported (*2,3*). Although muscle uptake anywhere in the body may constitute a diagnostic dilemma, the abundance of small muscle groups in the neck poses a particular problem in scanning patients with suspected head and neck neoplasms and lymph node disease. During the course of routine PET scanning for a variety of tumors, we observed variable uptake of activity in the midline of the neck on both localized head and neck and whole-body scans. The purpose of this study was to evaluate the premise that the focal uptake observed in the region of the larynx was due to laryngeal muscle activity.

MATERIALS AND METHODS

The study group consisted of 24 consecutive patients (16 women, 8 men; aged 31–91 yr, mean age of 52 yr) who underwent FDG-PET whole-body scanning for nonhead and neck cancers (8 lymphoma, 5 breast carcinoma, 4 sarcoma, 3 melanoma, 2 lung carcinoma, 1 multiple myeloma, 1 teratoma). The patients were randomly divided into two groups. The first group was asked to remain absolutely silent throughout the PET study starting from 5 min prior to the injection until the end of the study. The second group was asked to read aloud or talk to the accompanying person for at least 5 min before the injection, during the injection and 10 min after the injection. Three patients who were randomized to the speaking group did not comply fully with instructions and spoke only intermittently during this period.

FDG was prepared using the method described by Hamacher et al. (*4*). All patients fasted for 6 hr before the PET study and were injected with 350 MBq (9.5 mCi) FDG intravenously. Scans were obtained on a whole-body PET scanner. Thirty-one slices were produced over a 10.6-cm axial field of view. Whole-body images were acquired starting 40 min postinjection by obtaining 10 consecutive 5-min images from the patient's head to below the pelvis. The complete set of 310 image planes were reconstructed and smoothed in the axial direction to obtain a single three-dimensional dataset with a spatial resolution of 12 mm; 10-min transmission scans with ^{68}Ge rod sources were used for attenuation correction of emission scans for the localized views. Twenty patients had either half-body or whole-body FDG scans, four patients had only localized views of the head and neck region. Any patients who did not have localized emission scans that included the neck region as part of their clinical investigation had extra emission views of the neck acquired at the end of the scanning session. Images of the neck were analyzed by visual inspection of FDG activity distribution in the tomographic slices and uptake in the laryngeal region was evaluated using the criteria summarized in Table 1. For those patients in whom the brain was not imaged (four patients), only surrounding soft-tissue uptake was used as a reference.

One of the patients had a MRI study of the head and neck performed the same day. The PET study was registered to the MRI study using a point-based registration technique using internal anatomical landmarks (*5*). The landmarks used for registration include the bases of the cerebellar hemispheres, inferior temporal lobes, anterior aspect of the mandible and the odontoid peg of the axis vertebra. The root mean square error of these corresponding points in the PET and MRI studies was 3.1 mm. This registered study was used to precisely localize the site of laryngeal muscle uptake.

All studies were reviewed blindly by two nuclear medicine physicians and a consensus result was reached for uptake grade in the laryngeal region for each patient. PET findings were then correlated with the patients' randomization category.

RESULTS

PET findings in the region of the larynx are summarized in Table 2. All 11 patients who fulfilled the study requirements for 'speaking' had grade 2 uptake in the laryngeal region: 10 patients had high-grade and 1 patient had intermediate grade. The three patients who spoke intermittently had grade 1 uptake.

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TABLE 1
Classification Criteria for Grade of FDG Uptake in the Laryngeal Region

Grade	FDG uptake
0	No detectable increased uptake in the region of the larynx
1	Equivocal or low-grade uptake (slight increase above the level of surrounding soft tissue)
2	Intermediate to high-grade uptake (equal to or greater than brain uptake and/or very much greater than adjacent soft tissue

In 9 of the 10 patients who remained silent during the study, there was grade 0 uptake in the region of the larynx. The one patient classified as having grade 1 uptake had equivocal increased uptake in the laryngeal region in which the grade of FDG uptake was only marginally higher than the surrounding soft tissue. As for those patients in whom only localized views of the neck were obtained without acquisition of brain images (four patients), three of the four were randomized to remain silent and did not have any detectable uptake. The fourth patient who was placed in the speaking group had intense laryngeal uptake. Even in the absence of the brain as one of the reference organs, the intensity of uptake was clearly high grade.

The registered PET-MRI study performed on the one patient, who was in the speaking group, revealed the paired muscles visualized in the FDG study to be located posterior to the thyro-cricoid cartilage in an area which corresponded to the posterior cricoarytenoid muscles (Fig. 1). The patient data, however, indicated that the site of FDG uptake could vary from a posterior to an anterior position in relation to the thyro-cricoid cartilage. This variation may be due to activation of different intrinsic muscles of the larynx, with preferential uptake in different muscles depending on whether adduction or abduction was the dominant action during phonation. These various muscles include the posterior cricoarytenoid, lateral, oblique, transverse cricoarytenoids and the cricothyroid (Fig. 2).

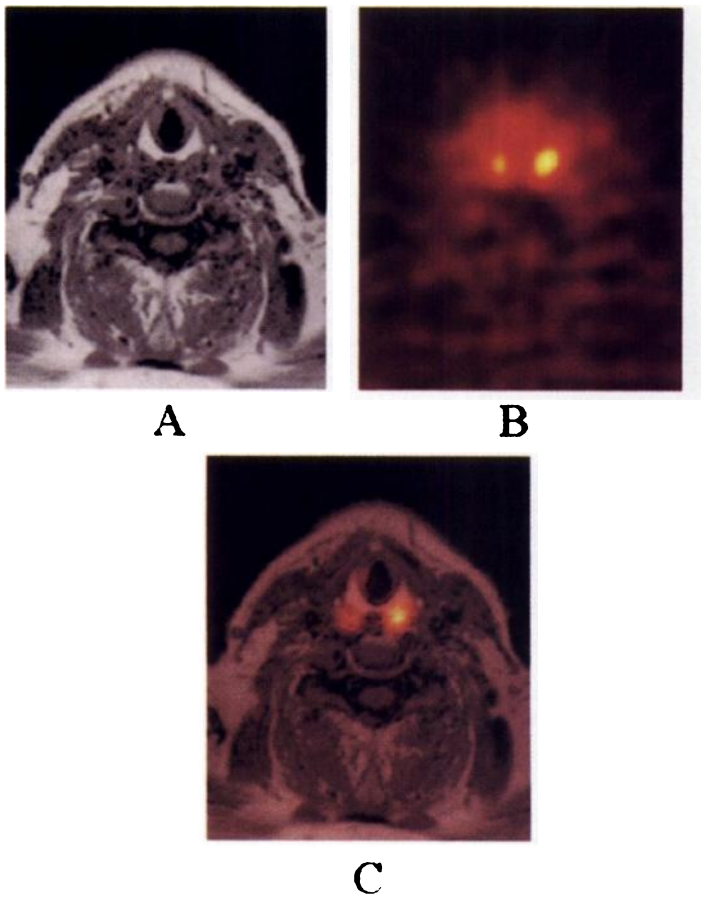

FIGURE 1. A transaxial T1-weighted MR image displayed in gray intensities (A) and a PET image in hot metal scale (B) are shown. A registered PET- MRI transaxial image in overlay display (C) in a 'speaking' patient demonstrates paired muscle uptake of FDG posterior to the thyro-cricoid cartilage in an area corresponding to the posterior cricoarytenoid muscles. Contraction of the posterior cricoarytenoid muscles abduct the vocal cords.

DISCUSSION

The larynx as a sphincteric device and an organ of phonation is rich in musculature. FDG appears to accumulate in striated muscle in the larynx in proportion to its contractile activity during speech. In the clinical setting, especially in patients with head and neck tumors, differentiating physiological uptake from viable tumor uptake is of critical importance. Although normal distribution of FDG (*6*) and tumor FDG-PET studies (*7,8*) in the extracranial head and neck region have been evaluated, laryngeal muscle uptake has not been reported. Our study indicates that when the laryngeal muscles are stimulated during movement of the vocal folds, activation-induced FDG uptake is observed reflecting local glucose metabolism. Our findings may have differed from these earlier studies because the patients were asked to vocalise during the uptake period. The exact site of FDG uptake appeared to vary between patients with some showing uptake predominantly anteriorly and others posteriorly to the thyro-cricoid cartilage. This probably indicates the use of different muscles with varying forms of phonation.

A rigorous approach should be adopted to prevent physiological uptake of tracer in laryngeal muscles as it may lead to false-positive results. Based on these findings, we have now implemented a policy of requesting patients with head and neck malignancy to remain completely silent during the injection and uptake period of FDG.

With further refinement of our understanding of physiological FDG uptake in different laryngeal muscles during phonation, PET may prove to be a useful technique for investigating speech disorders.

TABLE 2
Patients in Each Grade Category Versus Speech

Grade	Speaking	Intermittently speaking	Silent
0	—	—	9
1	—	3	1
2	11	—	—

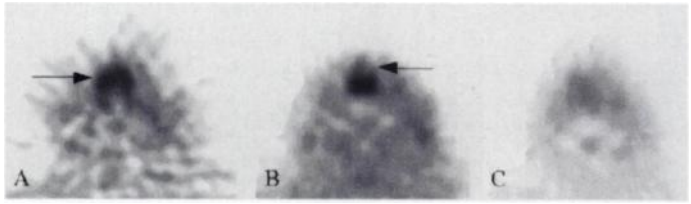

FIGURE 2. Transaxial FDG attenuation corrected emission views show grade 2 uptake predominantly anterior to the thyroid cartilage (A) and posterior to the thyroid cartilage (B) in 'speaking' patients due to activation of different intrinsic muscles of the larynx during phonation. The arrows indicate the coronal plane of the thyroid cartilage. No increased uptake, or grade 0 uptake is seen in a patient who was silent during the study (C).

CONCLUSION

The pattern of the physiological distribution of FDG within laryngeal muscle during phonation is important to recognize to enable differentiation of physiological from pathological uptake, particularly in the assessment of patients with head and neck tumors. The uptake in laryngeal muscles may have future application for the investigation of patients with speech disorders.

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Advantages of SPECT in Technetium-99m-Sestamibi Parathyroid Scintigraphy

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We demonstrate several advantages of SPECT in parathyroid scintigraphy. **Methods:** Forty-four parathyroid ^{99m}Tc-MIBI scintigrams were obtained before surgery in 43 patients suffering from hyperparathyroidism. For each patient, we obtained dynamic views and planar and SPECT images of the neck and thorax. For 15 patients, we also acquired a delayed static view of the neck 2 hr after tracer injection. Abnormal thyroid-area glands were detected with factor analysis of dynamic structure (FADS) of the initial dynamic acquisition. In the 15 patients with delayed views of the neck, we compared FADS and the double-phase study results to detect glands in the thyroid uptake area. Glands outside the thyroid area were demonstrated on planar views. The location of enlarged glands was more precisely defined on the tomographic slices. The anatomic and histologic findings and the evolution of hypercalcemia after surgery were taken as reference. **Results:** Sixty-four abnormal glands were found during surgery, including 39 observed in patients who underwent reoperation for persistent or recurrent hyperparathyroidism. Twenty-two of these glands were in an abnormal location, including 10 in the mediastinum. SPECT allowed the detection of three glands not demonstrated on planar views or FADS. Fifty-eight glands were correctly localized scintigraphically, including 34 in patients who underwent reoperation. Therefore, SPECT raised the sensitivity from 86% to 90.5% and from 79.5% to 87% in the reoperated patients. Tracer uptake in the low mediastinal area was better analyzed on tomographic slices than on planar views. Only seven false-positive results were depicted by planar views or FADS; none were depicted on SPECT. **Conclusion:** A combination of FADS and SPECT permits detection of small glands, even in a posterior location, inside or outside the thyroid area. This scintigraphic method enables the surgeon to define more precisely details about the location of the enlarged gland and contributes to improved parathyroid surgery.

Key Words: parathyroid scintigraphy; technetium-99m-sestamibi; SPECT; FADS

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Expert parathyroid surgeons can cure 95% or more patients with hyperparathyroidism, even without any preoperative localization study, in cases of primary surgery (*1,2*). In contrast, parathyroid surgery for recurrent or persistent hyperparathyroidism, is much more difficult (*3,4*) and less successful. Granberg et al. (*5*) calculated a surgical success rate of 85% in a compilation of 550 reoperated patients.

In the case of reoperation for persistent or recurrent hyperparathyroidism, the proportion of glands at unusual sites is large: 72% in a series of 112 reoperations (*6*) and a cumulative

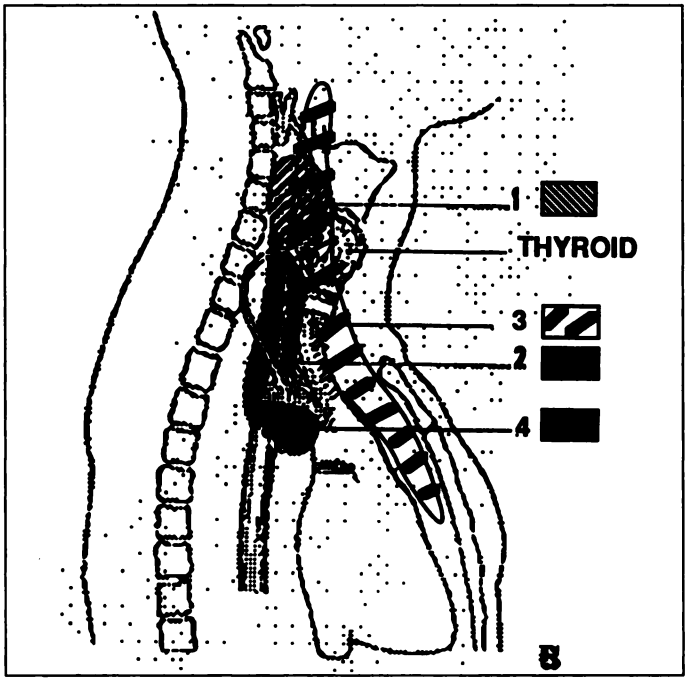

FIGURE 1. Localization of (1) normal and (2) abnormal posterosuperior glands and (3) anteroinferior glands. (4) Middle mediastinum area.

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