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# $^{18}\text{F}$ -FDG PET of Patients with Hürthle Cell Carcinoma

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Hürthle cell carcinoma is an uncommon differentiated thyroid cancer characterized by an aggressive clinical course and low avidity for  $^{131}\text{I}$ . Treatment usually involves an aggressive surgical approach often combined with  $^{131}\text{I}$ .  $^{18}\text{F}$ -FDG PET has been helpful in the staging and evaluation of many types of aggressive malignancy. No reports to date have described the utility of PET in a series of patients with Hürthle cell cancer. We reviewed our experience with  $^{18}\text{F}$ -FDG PET in the care of patients with Hürthle cell carcinoma to determine the likelihood of uptake in these cancers and the effect of  $^{18}\text{F}$ -FDG PET on patient care.

**Methods:** Patients with Hürthle cell cancer who were seen between June 2000 and April 2002 and were imaged with  $^{18}\text{F}$ -FDG PET were included. Imaging and clinical data were reviewed. PET results were compared with the results of anatomic imaging (CT, sonography, or MRI) and  $^{131}\text{I}$  imaging when performed. Patient charts were reviewed to identify any change in management that resulted from the  $^{18}\text{F}$ -FDG PET findings.

**Results:** Fourteen  $^{18}\text{F}$ -FDG PET scans of 12 patients were obtained in the time frame indicated. All patients had documented Hürthle cell carcinoma. PET showed intense  $^{18}\text{F}$ -FDG uptake in all known Hürthle cell cancer lesions but one. PET showed disease not identified by other imaging methods in 7 of the 14 PET scans. PET identified distant metastatic disease (5) or local disease (2) that was more extensive than otherwise demonstrated. In 7 of the 14 scans, the information provided by PET was used to guide or change therapy. **Conclusion:** Hürthle cell carcinoma demonstrates intense uptake on  $^{18}\text{F}$ -FDG PET images. PET improves disease detection and disease management in patients with Hürthle cell carcinoma relative to anatomic or iodine imaging.  $^{18}\text{F}$ -FDG PET should be recommended for the evaluation and clinical management of patients with Hürthle cell carcinoma.

**Key Words:** thyroid neoplasms; emission CT; PET; Hürthle cell cancer

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**H**ürthle cell carcinoma is an aggressive, follicular thyroid cancer variant that is infrequent relative to papillary or follicular thyroid malignancy. The tumor is derived from

follicular cells and is composed mostly of oxyphilic follicular cells (1). Hürthle cell cancer has a 33% risk of metastasizing distantly, compared with 22% for follicular and 10% for papillary cancer. Survival at 5 and 20 y is poorer for patients with Hürthle cell cancer. Papillary and follicular cancer patients have survivals of 94% and 87%, respectively, at 5 y and 87% and 81%, respectively, at 20 y, whereas Hürthle cell cancer patients have survivals of 81% and 65% at 5 and 20 y, respectively (2).

The diagnosis of Hürthle cell carcinoma, as with all follicular cancers, requires histologic identification of malignant characteristics to separate adenomas from carcinomas. Ideally, an initial complete resection with preservation of laryngopharyngeal function is combined with appropriate adjuvant therapy. Unfortunately, Hürthle cell neoplasms have poor iodine accumulation, and therefore,  $^{131}\text{I}$  therapy is not often a good therapeutic option (3). Local recurrence requires a careful balance of revision surgery and, potentially, external-beam radiation therapy. External-beam radiation therapy has also benefited nonpulmonary distant metastasis. Complete resection of the primary and any cervical disease, thorough evaluation for distant metastasis, and close follow-up for local or distant recurrence would be prudent.

Several functional imaging modalities have been proposed for imaging Hürthle cell cancer (3–5). Imaging with  $^{99\text{m}}\text{Tc}$ -sestamibi,  $^{99\text{m}}\text{Tc}$ -dimercaptosuccinic acid, and  $^{111}\text{In}$ -diethylenetriaminepentaacetic acid-D-Phe1-octreotide has shown encouraging results.  $^{18}\text{F}$ -FDG PET can identify high-grade cancer because of the high glucose uptake in aggressive, poorly differentiated malignancy. Although  $^{18}\text{F}$ -FDG PET has reduced sensitivity for early-stage, well-differentiated thyroid malignancy (6), improved sensitivity is seen in aggressive, dedifferentiated,  $^{131}\text{I}$ -negative thyroid malignancy with  $^{18}\text{F}$ -FDG PET. The highly aggressive nature of Hürthle cell cancer may provide an opportunity to image this malignancy with improved sensitivity using PET. Indeed, reports of  $^{18}\text{F}$ -FDG PET in patients with Hürthle cell cancer have supported this notion (7–11). We reviewed our data of patients with  $^{18}\text{F}$ -FDG PET scans and Hürthle cell cancer of the thyroid to determine the sensitivity of PET in these patients and its contribution to their overall care.

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## MATERIALS AND METHODS

### Patients

Patients with Hürthle cell cancer seen between June 2000 and April 2002 who were imaged with  $^{18}\text{F}$ -FDG PET were included. The study was approved by the Mayo Clinic institutional review board, and clinical data were reviewed. All imaging results as indicated in the medical record were used as the imaging results for the study. Experts on each modality ( $^{131}\text{I}/^{123}\text{I}$ , CT, PET, or sonography) interpreted the imaging data. PET results were compared with the findings of other types of imaging ( $^{131}\text{I}/^{123}\text{I}$ , CT, or sonography), when performed. Imaging with  $^{131}\text{I}/^{123}\text{I}$  (7 patients) was performed on average within 7 d (range, 23 d before to 6 d after) of the PET scan. CT (10 patients) was performed on average within 1.8 d (range, 2 d before to 7 d after) of the PET scan. MRI (2 patients) was performed on average within 1.8 d (range, 7 d before to 2 d after) of the PET scan. Sonography (7 patients) was performed on average within 2.1 d (range, 8 d before to 5 d after) of the PET scan. CT was performed on a HiSpeed CT/i tomograph (General Electric Medical Systems) and included the area from the zygoma to the aortic arch when neck scans were obtained. Generally, sonography was the primary anatomic imaging technique used for the neck. CT of the chest was performed on all but 3 patients as well. Contrast (100 mL of Omnipaque 350; Amersham Health) was injected intravenously, and helical imaging was started 30 s afterward using 5-mm collimation. Scans of more superior regions, to include the skull base, were obtained when indicated. MR images were obtained on a limited basis.  $^{131}\text{I}$  imaging was performed 24 h after the administration of 111–148 MBq (3–4 mCi) of orally administered  $^{131}\text{I}$ . Whole-body images and dedicated neck views were obtained. Imaging was performed on a Bodyscan tomograph (Siemens Medical Systems, Inc.).

Patient charts were reviewed to identify any change in management that resulted from the  $^{18}\text{F}$ -FDG PET findings indicated by the physician. Disease limited to the thyroid gland was treated with a near-total or total thyroidectomy. Suggestive lymph nodes identified either radiologically or clinically were addressed with regional lymphadenectomy. Extrathyroidal extension required frozen-section control of margins to guide resection of tumor invasion of the larynx, trachea, esophagus, or other vital neck structures.

### PET

$^{18}\text{F}$ -FDG PET was performed on an Advance tomograph (General Electric Medical Systems). This tomograph has an axial field of view of 15 cm and an axial resolution of 5.4 mm from a point source at a 10.0-cm radius.

The  $^{18}\text{F}$ -fluoride was produced by a Trace cyclotron (General Electric Medical Systems) that is on site.  $^{18}\text{F}$ -FDG was synthesized by the Hamacher method.  $^{18}\text{F}$ -FDG was tested for sterility, pyrogenicity, and radiochemical purity on each production run.

PET emission images of the body, to include the head, neck, chest, and abdomen, were obtained 50 min after intravenous injection of 370–740 MBq of  $^{18}\text{F}$ -FDG. After the patients had been allowed to void, they were positioned on the tomographic gantry and a series of body images was obtained. This set of image data spanned at least from the upper orbit to the iliac crests.

Emission images were reconstructed using filtered backprojection with a Hann window of 5.0-mm width and iterative reconstruction. Attenuation correction was used. Emission data were corrected for scatter, random events, and dead-time losses using the manufacturer's software. Image pixel size was 4.25 mm, and the image was displayed in a 128 by 128 matrix. Standard tomo-

graphic views and a maximum-intensity projection were reviewed during scan interpretation.

### Data Analysis

Results from PET and other imaging methods were tabulated. The results of the imaging tests were compared, and differences in disease distribution observed in the different imaging studies were noted. The imaging results were compared with pathologic sampling of regions of concern. The sensitivity of  $^{18}\text{F}$ -FDG PET was determined through histologic confirmation or through clinical consensus on disease status based on the medical record.

## RESULTS

Fourteen  $^{18}\text{F}$ -FDG PET scans of 12 patients were obtained in the time frame indicated. Ten of the PET scans were for evaluation of morphologic abnormalities found by other imaging techniques. Of the other 4 patients, 2 were imaged without any other suspected abnormalities, 1 for a positive finding on physical examinations, and 1 for an elevated thyroglobulin level. The patient group included 7 men and 5 women with an average age of 47 y (range, 38–78 y). All patients had previous biopsy-proven Hürthle cell carcinoma. Eleven of the 12 patients were being evaluated for recurrent Hürthle cell carcinoma, and 1 patient was undergoing disease staging for the planning of initial therapy. In patients with previous disease, the mean time from diagnosis to the time of evaluation was 4.4 y (range, 5 mo to 15 y). At the time of evaluation, Hürthle cell carcinoma was shown to be present in 13 patients, as confirmed by pathology in 10 and by clinical follow-up in 3. One patient (patient 7), who had undergone subtotal thyroidectomy 1 mo before, was shown to be disease free on all imaging tests except iodine imaging, which was equivocal; was biopsy negative in the neck by fine-needle aspiration; and was disease free 1 y later on follow-up. PET findings were positive, with intense  $^{18}\text{F}$ -FDG uptake, in all but 1 of these 13 patients with known disease (92% sensitivity).

Disease not identified by other imaging methods was shown in 7 of the 14 PET scans obtained (Table 1). PET identified distant metastatic disease (6) or local disease (2) that was more extensive than otherwise demonstrated (1 patient had both more extensive local disease and distant disease shown by PET). Of these 8 areas of disease, 5 were proven by biopsy, 2 were confirmed by other imaging methods, and 1 was considered positive on the basis of other clinical data (Figs. 1 and 2). For 7 of 14 scans, the information provided by PET was used to guide or change therapy. Of 7 patients who had iodine scans, 6 had negative findings and 1 scan was read as questionable. In the 1 PET scan that was read as negative, there was substantial nonspecific neck uptake, probably because of muscle or fat uptake, that may have obscured the 1 focal site of disease then thought to exist (Fig. 3). The focus as seen on sonography was  $1.8 \times 1.1 \times 0.9$  cm. Three months later, this site was resected and proven to be grade 2/4 Hürthle cell recurrence. On retrospective review of the PET data, the area in

**TABLE 1**  
Patient Data

Patient no.	Sex	Findings								PET effect
		PET		CT		Neck sonography	<sup>131</sup> I/ <sup>123</sup> I	Pathology		
		Local	Distant	Local	Distant					
1	M	Neg	Pos	NA	Indeterminate	Neg	ND	Pos	Indeterminate lung nodule shown to be positive on PET	
2	M	Neg	Pos	NA	Pos	Neg	Neg	Pos	Much more extensive distant disease on PET	
3a	F	Neg	Pos	NA	Pos	Neg	Neg	Pos	Confirmed disease	
3b	F	Pos	Neg	NA	Neg	Pos	ND	ND (F/U pos)	Confirmed disease	
4	M	Neg	Pos	NA	Pos	Pos	Neg	ND (F/U pos)	Confirmed disease	
5	F	Neg	Pos	NA	Pos	Neg	ND	ND (F/U pos)	Confirmed disease	
6	M	Neg	Pos	NA	Pos	Neg	ND	Pos	Confirmed disease	
7	F	Neg	Neg	NA	Neg	Neg	Indeterminate	Neg	Confirmed disease	
8	M	Neg	Pos	ND	ND	Neg	Neg	Pos	Showed unknown distant disease (pelvis)	
9	F	Neg	Neg	Neg	Neg	Pos	ND	Pos	PET falsely read as negative	
10	F	Pos	Pos	Neg	Neg	NA	ND	Pos	Showed unknown distant disease (mediastinum)	
11	M	Pos	Pos	Pos	Neg	Neg	ND	Neg (pleural fluid)	Suspected metastatic disease from PET: treated	
12a	M	Pos	Pos	Pos	Indeterminate	Pos	Neg	Pos	Indeterminate lung nodules shown to be positive on PET	
12b	M	Pos	Neg	Neg	Indeterminate	Indeterminate	Neg	Pos	Active local disease seen on PET only	

Neg = negative result; Pos = positive result; ND = not done; F/U pos = follow-up considered active disease to be present.

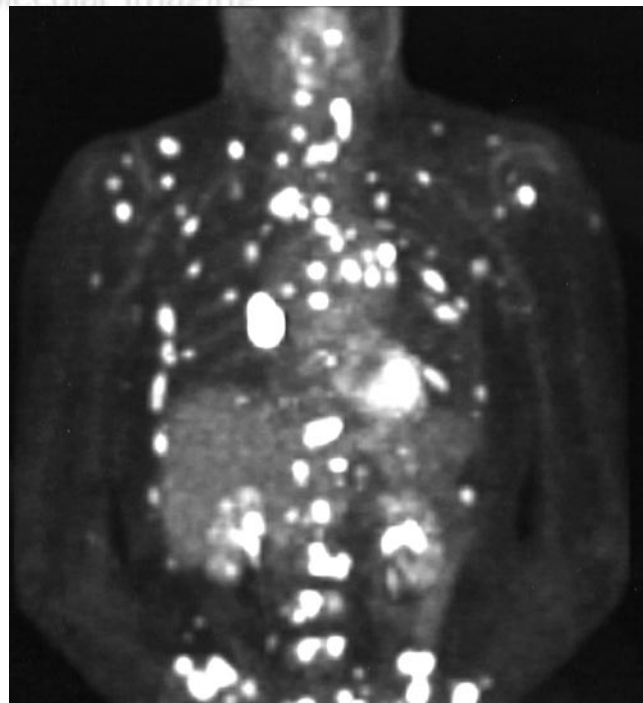
question did show moderate metabolism, but the finding was not obvious.

## DISCUSSION

Hürthle cell carcinoma is an aggressive thyroid cancer that may require more aggressive locoregional therapy than other thyroid malignancies. This tumor is more commonly metastatic, and a thorough evaluation for distant metastasis is recommended. Hürthle cell carcinoma is also quite rare, with little published on imaging of this malignancy with PET.

In this review, we have shown that <sup>18</sup>F-FDG PET is likely to show regions of active involvement by Hürthle cell cancer. Most areas of tumor demonstrated intense <sup>18</sup>F-FDG uptake that was similar in intensity to that seen in other highly metabolically active malignancies. In the 1 case that was falsely negative on PET, other confounding uptake of <sup>18</sup>F-FDG in the neck may have hampered the detection of a small focus (1 cm) of disease. The disease in this case was also of low grade (2/4), possibly reducing <sup>18</sup>F-FDG uptake. Retrospective review of this case showed that moderate uptake was present in the region of the disease but was difficult to detect. New advances such as PET/CT fusion may improve the accuracy of PET in such cases.

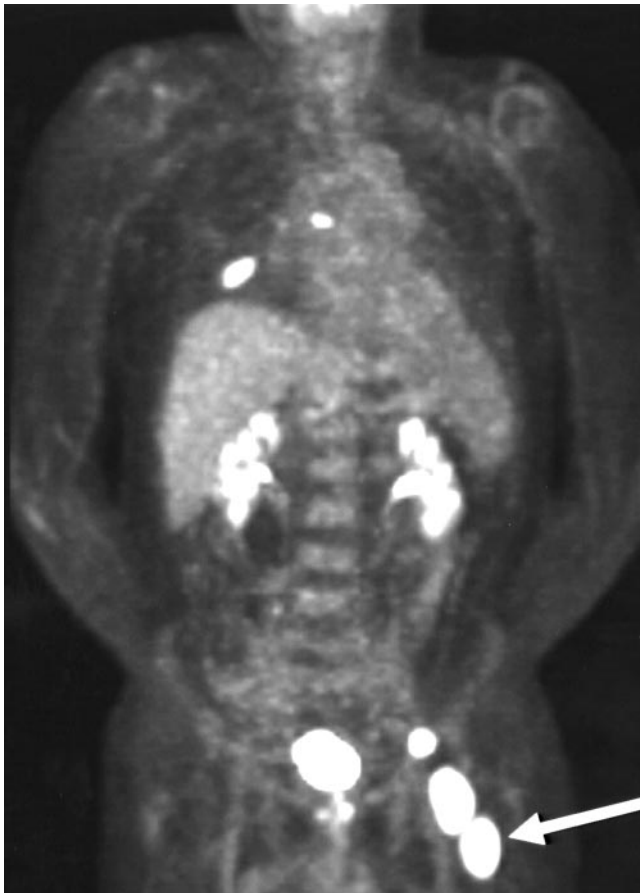
PET provided additional information on disease extent that led to a change in patient care for 50% (7/14) of the scans obtained. The change in care was due to better char-



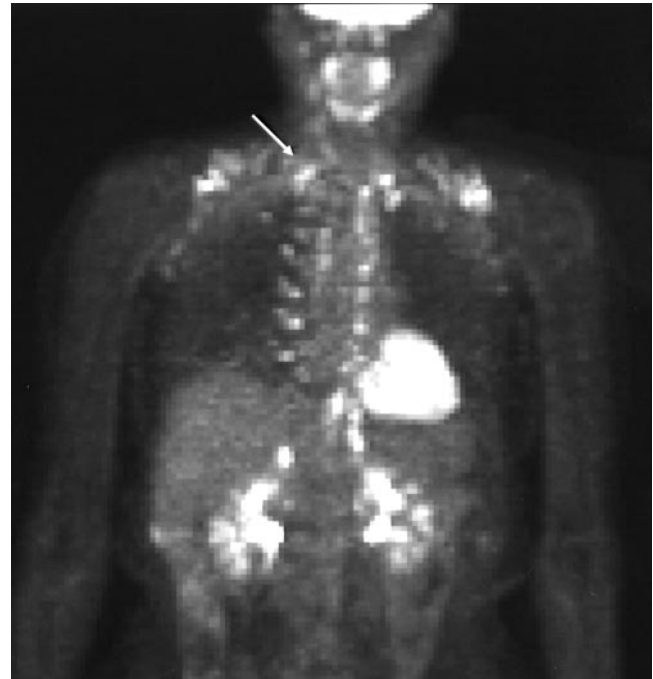
**FIGURE 1.** PET image of patient 2, who had history of Hürthle cell cancer and returned with complaint of diffuse aches. Single indeterminate lung nodule with some mediastinal adenopathy was seen on CT. Sonography and <sup>131</sup>I scans had negative findings. PET image showed widespread bone and lung metastases, which were confirmed with right hilar biopsy.

acterization of indeterminate abnormalities on CT or sonography for 3 scans and to detection of unsuspected disease for 4 scans. The contribution of PET in the patient group was dramatic and certainly comparable with other data reporting clinical management changes resulting from PET in other  $^{18}\text{F}$ -FDG-avid malignancies such as colorectal and lung cancer (12). Our data support the results of Plotkin et al. (11), who described accurate identification of Hürthle cell carcinoma by  $^{18}\text{F}$ -FDG PET in a group of 17 patients with indications of recurrent disease.

Our data are limited in that the number of patients in our study was low. However, considering that this malignancy is uncommon, larger groups of patients will be difficult to obtain. Another limitation is that this study was a retrospective review, with all the inherent biases of such. Referral of these study patients for PET may well have been prompted by existing clinical dilemmas. The high rate with which PET affected management could thereby be somewhat exaggerated and might not be seen in a group of patients who are referred prospectively.



**FIGURE 2.** PET image of patient 8, who had Hürthle cell cancer previously treated and who returned with elevated thyroglobulin level (800 ng/mL) for evaluation. Neck sonography and  $^{131}\text{I}$  scan had negative findings. PET image showed lung, vertebral body, and pelvis/femur (arrow) metastases. Biopsy of pelvis confirmed metastatic disease.



**FIGURE 3.** PET image of patient 9, who had Hürthle cell cancer previously treated and who returned for follow-up evaluation. Neck sonography showed 1-cm right-neck lymph node suggestive of Hürthle cell cancer. PET image showed variable nonspecific uptake in neck and chest, and no definite tumor was believed to be present. Biopsy 2 mo later of region seen on sonography confirmed disease (2/4 grade Hürthle cell cancer), which was also likely near right-lower-neck uptake seen on PET (arrow).

## CONCLUSION

Hürthle cell carcinoma demonstrates intense uptake on  $^{18}\text{F}$ -FDG PET. Relative to anatomic or iodine imaging, PET improved staging and disease management in patients with Hürthle cell carcinoma.  $^{18}\text{F}$ -FDG PET should be recommended for the evaluation and clinical management of patients with Hürthle cell carcinoma.

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