The Journal of Laryngology and Otology
June 1999, Vol. **113,** pp. 548–554

The diagnostic value of positron emission tomography (PET) with radiolabelled fluorodeoxyglucose (^{18}F-FDG) in head and neck cancer

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Abstract
Positron emission tomography (PET) scanning has recently been introduced into clinical practice but its usefulness in the management of head and neck cancer is not well defined. The aim of this prospective preliminary study was to examine the clinical value of fluorodeoxyglucose (FDG) – PET in patients with head and neck cancer treated by radiotherapy with surgery in reserve by (i) relating quantitative uptake of isotope to tumour type and histological grade and (ii) comparing the imaging findings of PET and magnetic resonance imaging (MRI) in post-radiotherapy assessment of tumour response. Twenty-one patients had pre-treatment PET and MRI scans and these were repeated four and eight months after treatment if there was no clinical relapse. Pre-treatment uptake of FDG using tumour to cerebellar ratio parameters was significantly related to the histological grade of squamous cancer ($p = 0.04$) but not to tumour type. Discordance of post-treatment PET/MRI findings in one case indicates a possible role for PET in the early detection of tumour recurrence. Other potential uses of PET scanning in the management of head and neck cancer are discussed.

Key words: Tomography, emission-computed; Head and neck neoplasms

Introduction

Large tumours of the head and neck region are well visualized using anatomically based imaging techniques such as computerized tomography (CT) and MRI. Following radiotherapy for head and neck cancer, normal tissue morphology is often disrupted so that differentiation of viable tumour from radition-induced change using CT/MRI is difficult. This may in practice lead to the serious clinical problems of: (i) a critical delay in the diagnosis of recurrence, (ii) normal tissue necrosis precipitated by repeat deep diagnostic biopsies and even (iii) cancer-free organ resection because of diagnostic uncertainty. Physiological imaging using PET with radiolabelled fluorodeoxyglucose (^{18}F-FDG) has already been shown in several studies to be useful in evaluating response of head and neck cancer to radiotherapy (Chaiken *et al.*, 1993; Greven *et al.*, 1994; Bailet *et al.*, 1995; Wong *et al.*, 1997). These studies used the traditional design of PET system based on multiple rings of bismuth germanate crystals; they did not use a prospective and systematic comparison of PET with MRI related to clinical outcome.

This study has used an alternative PET camera based on large area multi-wire gas chambers referred to as high density avalanche chambers (HIDAC) detectors (Townsend *et al.*, 1987). The system had previously demonstrated good characteristics for tumour imaging in small animals, (Hastings *et al.*, 1996) primarily due to the high intrinsic spatial resolution. This advantage allied to its considerably lower cost compared to commercially available crystal PET systems made it attractive for clinical imaging. The aims of this small prospective study were to examine the potential clinical utility of PET scanning before and after radiotherapy, comparing its diagnostic value with MRI studies, as well as relating pre-treatment tumour activity to clinical outcome with the intention of providing useful prognostic information for the individual patient.

Patients and methods

Fifteen patients were selected with T2 to T4 head and neck squamous carcinomas suitable for definitive radiotherapy with surgery in reserve; in addition six patients with non-squamous histology were

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Accepted for publication: 12 March 1999.

TABLE I
PATIENT AND TUMOUR CHARACTERISTICS

	Patient					
	Sex	Age	Site	Stage	Pathology	Date XRT
1	M	58	Post tongue	T4N2	Poorly diff. SCC	Mar 95
2	M	63	Post tongue	T4N2	Poorly diff. SCC	Mar 95
3	M	62	Glottic larnyx	T2NO	Well diff. SCC	Apr 95
4	M	37	Nasal cavity	T4NO	Mod. diff. SCC	Jun 95
5	M	49	Post pharynx	T2NO	Mod. diff. SCC	Aug 95
6	M	47	Tonsil	T4N2	Mod. diff. SCC	Sep 95
7	F	45	Supraglottic larynx	T4NO	Poorly diff. SCC	Nov 95
8	F	37	Nasal cavity	T3NO	Well diff. SCC	Dec 95
9	M	55	Post pharynx	T2N2	Poorly diff. SCC	Jul 96
10	M	60	Supraglottic larynx	T3N2	Poorly diff. SCC	Jul 96
11	M	57	Supraglottic larynx	T3N1	Mod. diff. SCC	Sep 96
12	M	44	Tonsil	T2N2	Mod. diff. SCC	Oct 96
13	M	67	Post tongue	T4N2	Poorly diff. SCC	Jan 97
14	M	64	Neck nodes unknown primary	TXN2	Poorly diff. SCC	Feb 97
15	M	72	Post tongue	T2N2	Mod. diff. SCC	Jun 97
16	M	53	Supraglottic larynx	N/A	Plasmacytoma	May 95
17	M	46	Maxillary antrum	N/A	Melanoma	Jun 95
18	M	61	Maxillary antrum	T4NO	Carcinoma type not specified	Sep 95
19	F	66	Tonsil	T4NO	Adenocarcinoma	Dec 96
20	M	40	Temporal bone	N/A	Glomus	Feb 97
21	F	59	Supraglottic larynx	T4NO	Neuroendocrine carcinoma	Feb 97

(N/A: not applicable)

studied particularly to examine their pre-treatment quantitative measurements in comparison to those of the squamous cancers. Patients consented to having a baseline pre-treatment MRI scan and a PET scan within one week of each other as well as repeat PET and MRI scans four and eight months after radiotherapy if the patient remained clinically disease-free. All cases with suspected clinical or radiological recurrence had biopsy verification of disease status

PET scans were performed with a 60 minute acquisition time, 40 minutes after intravenous injection of 100 megabequerels of ^{18}F-FDG. 3-D acquisition and reconstruction produced an image of FDG distribution within a cylindrical field of view, 20 cm in diameter across the transaxial plane and 15 cm in length along the axis of the supine patient. The images were displayed as 5 mm thick consecutive 2-D slices in transaxial, coronal and sagittal planes. Uptake of FDG was determined using a method previously described for the HIDAC scanner (Moore *et al.*, 1998), which incorporates correction for the combined effects of attenuation and scatter. The FDG uptake in tumour was quantified using the tumour to cerebellar ratio. This was determined by delineating the tumour volume with the aid of an edge detection algorithm on each slice showing tumour uptake, to produce a 3-D region of interest (ROI). A representative cerebellar ROI was also determined on three consecutive slices. The ratio of tumour to cerebellar activity was then calculated

TABLE IIa
COMPARISON OF PET/MRI PREDICTION OF CLINICAL OUTCOME FOR 15 CASES OF SQUAMOUS CARCINOMA

				4 months post–XRT		8 months post–XRT		
Patient	Sex	Age	Local disease status	PET	MRI	PET	MRI	Outcome (analysis Jan 99) in months (m)
1	M	58	Recurrent nodes right block dissection (5 m)	–	+ ® neck	ND	ND	Died 19 m lung metastases
2	M	63	No recurrence	–	±	±	–	Alive and well 42 m
3	M	62	No recurrence	–	–	–	–	Intercurrent death 12 m
4	M	37	No recurrence	–	–	–	–	Alive and well 40 m
5	M	49	Primary recurrence Pharyngectomy (14 months)	+	–	+	–	Died disease 15 m
6	M	47	No recurrence	–	–	±	±	Alive and well 39 m
7	F	45	Residual primary Laryngectomy (4 months)	ND	ND	ND	ND	Died lung metastases 17 m
8	F	37	No recurrence	–	–	–	–	Alive and well 34 m
9	M	55	No recurrence	–	–	–	–	Alive and well 28 m
10	M	60	Residual neck nodes not fit for surgery	ND	ND	ND	ND	Died disease 7 m
11	M	57	No recurrence	–	–	–	–	Alive and well 27 m
12	M	44	No recurrence	–	–	–	–	Alive and well 25 m
13	M	67	No recurrence	–	–	–	–	Alive and well 23 m
14	M	64	No recurrence	–	–	–	–	Alive and well 23 m
15	M	72	Residual nodes ® block dissection (2 months) Path: non viable SCC	ND	ND	ND	ND	Alive and well 17 m

https://doi.org/10.1017/S0022215100144457 Published online by Cambridge University Press

TABLE IIb
COMPARISON OF PET/MRI PREDICTION OF CLINICAL OUTCOME FOR 6 NON-SQUAMOUS CASES

Patient	Sex	Age	Local disease status	4 months post–XRT PET	4 months post–XRT MRI	8 months post–XRT PET	8 months post–XRT MRI	Outcome (analysis Jan 99) in months (m)
16	M	53	Residual primary and metastases (myeloma)	+	+	ND	ND	Died disease 11 m
17	M	46	Not assessed	ND	ND	ND	ND	Rapidly progressive liver metastases, died 2 m
18	M	61	No recurrence	–	–	–	–	Alive and well 39 m
19	F	66	No recurrence	–	–	–	–	Intercurrent death (breast Ca) 10m
20	M	40	Stable	+	+	+	+	Alive and well 21 m
21	F	59	Primary recurrence Laryngectomy 15 months	+	+	ND	ND	Alive and well 23 m

+Significant scan abnormality; –No significant scan abnormality; ±Equivocal; ND not done (clinically inappropriate)

using (i) average counts per voxel in each ROI, (ii) maximum count in each ROI. The statistical relationships between these parameters and histology were examined for significance using a Kruskal-Wallis non-parametric test (Siegel, 1956).

A total of 52 PET and MRI scans were performed on the 21 patients, with 21 sets before radiotherapy and 31 sets post-treatment. The clinical characteristics of the patients are outlined in Table I. The MRI scans in three orthogonal planes used T1-weighted and T2-weighted spin echo sequences, performed with, and without, intravenous gadolinium contrast using a 1.0 Tesla magnet (Siemens Magnetom). Reporting of the PET scans (CDC) and MRI scans (RJJ) was conducted by appropriately qualified specialists, independently of each other.

Results

The patients and tumour characteristics are listed in Table I. The imaging features on both PET and MRI scans at four and eight months post external radiation therapy (XRT) for patients with squamous cell carcinoma are listed in Table II. Concordance between the two examinations was present in nine out of 12 patients (75 per cent) at four months and nine out of 11 patients (81 per cent) at eight months. The relationship of the imaging features to clinical outcome is also demonstrated. In the minority of patients where there was a discrepancy, one patient had a negative PET scan and an equivocal MRI scan at four months and vice versa at eight months; this patient was alive and well 42 months following initial diagnosis. One patient with a negative PET scan but a positive MRI scan at five months was too unwell to undergo either examination at eight months and died at 19 months from pulmonary metastases. Conversely, one patient had a positive PET scan at both four and eight months but a negative MRI on both occasions; this patient died at 15 months. All other patients demonstrated concordance both in terms of the imaging findings and their relationship to the clinical outcome.

Pre-treatment quantitative measurements were undertaken in 18 of 21 cases (Table III). In the squamous carcinoma group, tumour to cerebellar

TABLE III
RELATIONSHIP BETWEEN HISTOLOGY AND PRE-TREATMENT UPTAKE OF RADIO LABELLED FDG

Patient no.	Pathology	Index lesion	Volume (CM^3)	Tumour: Cerebellar ratio	
				Using voxel average	Using max counts
1	Poorly diff. SCC	T4	21.8	1.02	4.46
2	Poorly diff. SCC	T4	29.3	0.95	2.12
3	Well diff. SCC	T2	ES	ES	ES
4	Mod. diff. SCC	T4	32.4	0.43	2.73
5	Mod. diff. SCC	T2	22.6	0.76	3.48
6	Mod. diff. SCC	T4	23.4	0.68	4.03
7	Poorly diff. SCC	T4	23.4	1.37	5.66
8	Well diff. SCC	T3	8.2	0.63	3.58
9	Poorly diff. SCC	T2	7.2	0.90	3.40
10	Poorly diff. SCC	T3	16.4	ES	ES
11	Mod. diff. SCC	T2	18.3	1.17	6.85
12	Mod. diff. SCC	T2	5.0	0.79	3.45
13	Poorly diff. SCC	T4	44.5	1.24	6.96
14	Poorly diff. SCC	N2	25.8	1.66	11.55
15	Mod. diff. SCC	T2	ES	ES	ES
16	Plasmacytoma	N/A	42.0	2.35	9.84
17	Melanoma	N/A	48.6	0.60	6.61
18	Unspecified Ca	T4	12.7	0.84	3.96
19	Adenocarcinoma	T4	6.3	1.02	5.84
20	Glomus	N/A	13.6	1.37	6.27
21	Neuroendocrine ca	T4	89.9	1.36	9.88

N/A = not applicable; ES = equivocal scan.

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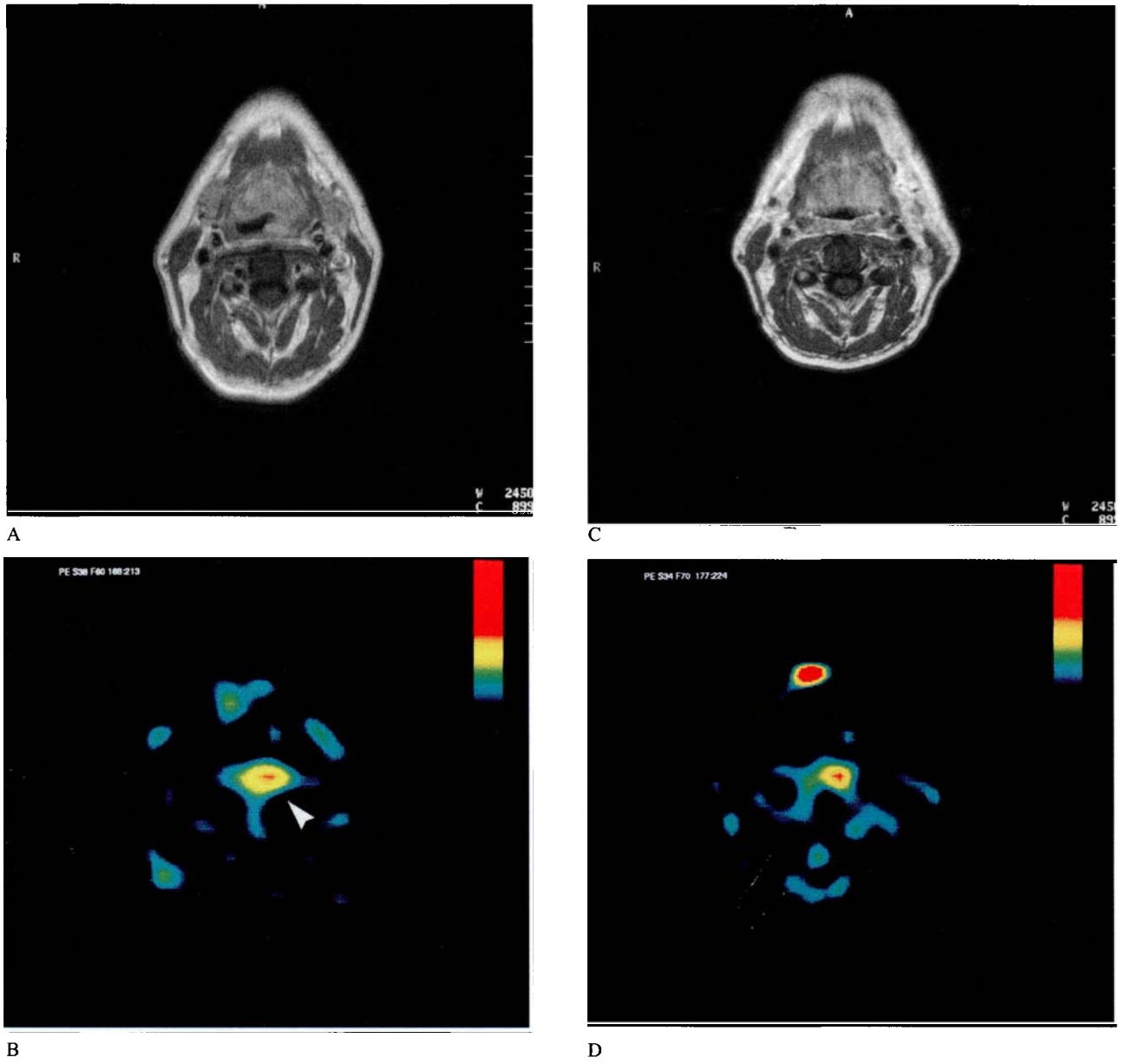

FIG. 1(a) Axial T_1 weighted MRI (post-contrast) at level of oropharynx demonstrates presence of a tumour mass arising from left oropharyngeal wall. (b) The corresponding axial PET-FDG image confirms active tumour in this region (arrow). (c) A repeat MRI obtained four months following commencement of radiotherapy demonstrates resolution of the mass. (d) The corresponding PET-FDG image continues to demonstrate abnormal isotope uptake. The focal area of increased uptake lying in the midline anteriorly represents a radioactive source attached to the chin. Clinical evidence of active tumour was demonstrated at eight months.

ratios derived from average counts per voxel showed a significant relationship with tumour grade ($p = 0.04$). There was no significant relationship between tumour grade and maximum ROI count. The uptake for well- and moderately-differentiated squamous carcinoma was less than for poorly-differentiated carcinoma. The six patients with non-squamous tumours (adenocarcinoma, neuroendocrine carcinoma, melanoma, plasmacytoma, glomus tumour and unspecified carcinoma) had a wide range of uptake values which fell within the range for squamous carcinoma except for the high voxel average value for plasmacytoma. As would be expected a significant difference was found between FDG-uptake volumes and tumour stage, with the values of T4 tumours being higher than for T2/T3 tumours ($p<0.05$ using a Mann-Whitney U non-parametric test).

Discussion

There is limited experience in the UK of the clinical utility of PET scanning in head and neck cancer. Squamous head and neck cancer characteristically has a high glycolytic rate which permits radiolabelled FDG to be used for imaging and quantification of uptake. This study has further confirmed that PET scanning can provide useful diagnostic information in head and neck cancer which should contribute towards improved patient management. Although there have been frequent claims for the value of PET in initial staging of head

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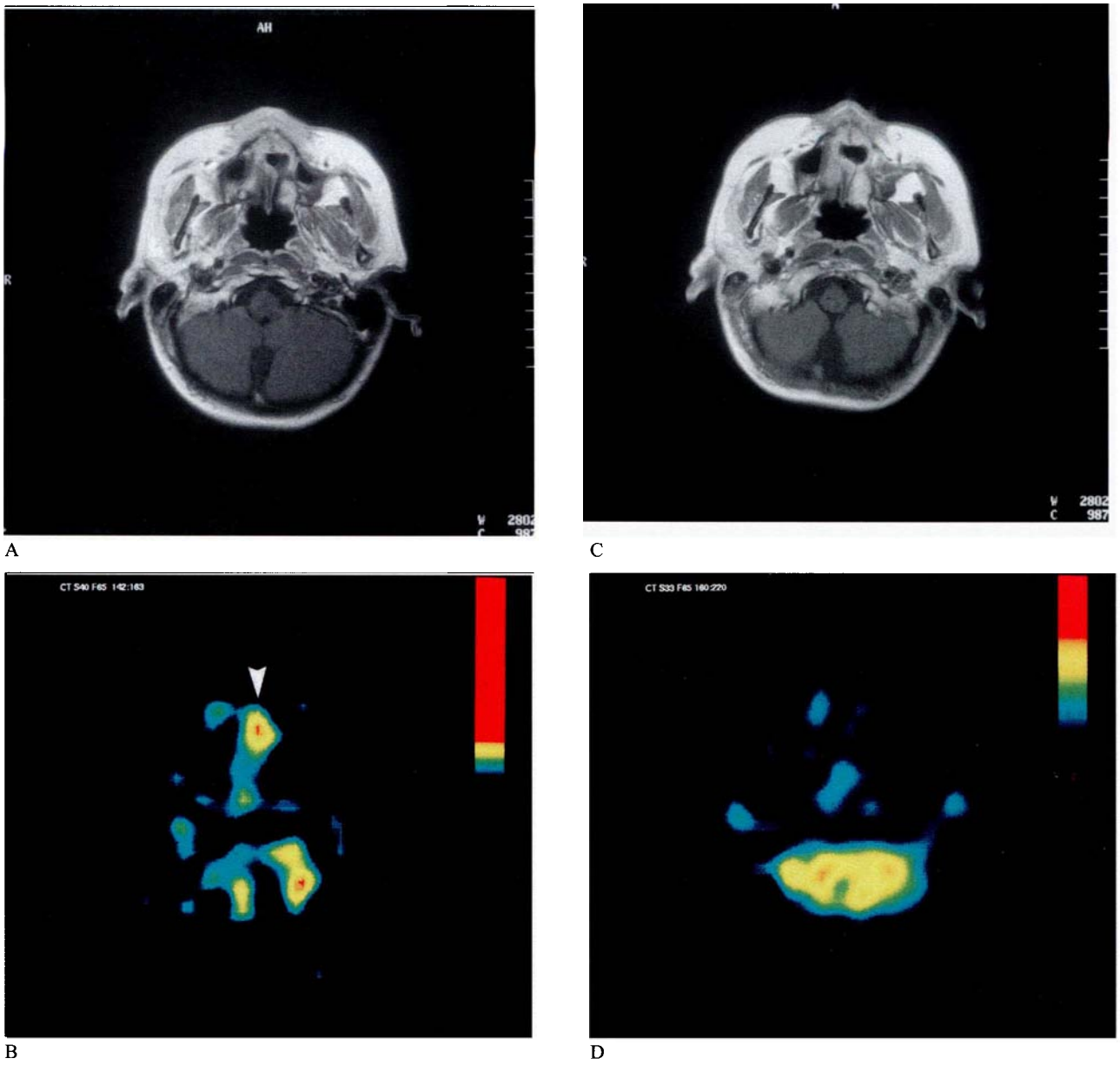

FIG. 2

(a) Axial T_1 weighted MRI (post-contrast) at level of hard palate demonstrating erosion with no associated tumour mass. (b) The corresponding PET-FDG image demonstrates abnormal isotope uptake in this region (arrow). (c) A repeat MRI scan obtained four months following commencement of radiotherapy demonstrates little overall change. (d) The corresponding PET-FDG image demonstrates resolution of abnormal focus previously present. The patient continues to remain well 31 months later.

and neck cancer (Braams *et al.*, 1995; Laubenbacher *et al.*, 1995; McGuirt *et al.*, 1995) it is unlikely that routine PET will supplant MRI/CT from this role. However, PET-FDG does have a worthwhile role in the detection of recurrent head and neck cancer after primary surgery or particularly following radiotherapy where the disruption of soft tissue planes makes interpretation of anatomically based scanning methods difficult (Bailet *et al.*, 1995; Anzai *et al.*, 1996). Moreover uptake of FDG seems to be useful in identifying occult head and neck cancers (Rege *et al.*, 1994; Mukherji *et al.*, 1996; Braams *et al.*, 1997). In our own study PET-FDG did help in the early detection of post-radiotherapy recurrent disease by virtue of its soft tissue discriminative ability. This can be seen from patient 5 (Figure 1) in which a positive PET scan predated clinical recurrence which was not predicted by a concomitant MRI scan. PET imaging also gave valuable additional information in the post-treatment assessment of patient 4 who had a persistent bone defect (Figure 2).

FDG uptake values have been found to be related to histological grade in some tumour types such as gliomas (Di Chiro *et al.*, 1982) and lymphomas (Leskinen-Kallio *et al.*, 1991). For head and neck cancer no study has hitherto reported a correlation between FDG uptake and histological grade. Two studies (Minn *et al.*, 1988; Haberkorn *et al.*, 1993) reported significant correlation between proliferative characteristics of head and neck squamous carcinoma and FDG uptake evaluated with PET. However in two studies (Minn *et al.*, 1988; Lauben-

https://doi.org/10.1017/S0022215100144457 Published online by Cambridge University Press

bacher *et al.*, 1995) there was no significant correlation between histological grade and FDG uptake. The current study demonstrates a clear relationship between uptake of isotope and histological grade of squamous carcinoma, albeit with small numbers; the parameter used to demonstrate this was tumour to cerebellar ratio using voxel averages (see Table III). This preliminary finding should be confirmed in larger studies. Although PET-FDG provides a non-invasive means of predicting histological grade it remains to be seen whether radiotherapy fractionation regimens should be altered to take account of this in terms of achieving a therapeutic gain in all cases.

Many studies have reported the ability of PET-FDG to identify the presence of node involvement (Rege *et al.*, 1994; Wong *et al.*, 1997) and this was confirmed in our study. This could potentially help radiotherapists to prescribe appropriate radiation doses to different compartments of the neck or help the surgeon decide on the type of neck dissection to be performed.

The capacity of PET-FDG to predict response to radiotherapy or chemotherapy is potentially its most useful role in head and neck cancer. Radiotherapy changes tumour proliferative characteristics and oxygen tension and these could both be assessed non-invasively during treatment thereby influencing prescription patterns. PET permits examination of tissue pharmacodynamics following chemotherapy and this is currently one of the most intriguing techniques in detecting sub-clinical response to cancer therapy (Haberkorn *et al.*, 1993; Price and Jones, 1995). Management could be influenced by accelerating radiotherapy regimens if high tumour proliferative rates are demonstrated during treatment, adding hypoxic cell cytotoxic or sensitizers such as Mitomycin C or Nimorazole if low oxygen tensions are detected, and choosing appropriate synchronous chemotherapy depending on demonstrable drug access to tumour in vivo.

The HIDAC PET system used for this study has confirmed its ability to demonstrate primary and nodal head and neck cancer. Although spatial resolution was satisfactory the low sensitivity of the system resulted in long acquisition times which are both technically and clinically inconvenient. Consequently future studies in this hospital will be conducted with a traditional BGO crystal-based system.

In this pilot study PET has demonstrated its potential application in both diagnostic and prognostic roles. Discordance between PET and MRI findings illustrates a potential utility in detecting recurrence following radiotherapy, thereby allowing early surgical salvage. False-positive PET and MRI findings demonstrates that there is no ideal imaging modality for post-radiotherapy assessment. Our study also found a relationship between quantitative uptake for isotope and histological grade that, if confirmed in larger studies, could in future permit individualization of radiotherapy prescription related to tumour proliferative characteristics.

Acknowledgements

This study was generously funded by North West Region Research and Development Directorate. We wish to thank Dr Alan Jeavons of Oxford Positron Systems for his advice and provision of the HIDAC detectors.

Special thanks to Miss Jenny Pursell for preparing the manuscript and the Department of Medical Illustration for the figures.

References

Anzai, Y., Carroll, W. R., Quint, D. J., Bradford, C. R., Minoshima, S., Wolf, G. T., Wahl, R. L. (1996) Recurrence of head and neck after surgery or irradiation: prospective comparison of 2-deoxy-2-[F-18] fluoro-D-glucose PET and MR imaging diagnoses. *Radiology* **200(1):** 135–141.

Bailet, J. W., Sercarz, J. A., Abemayor, E., Anzai, Y., Lufkin, R. B., Hoh, C. K. (1995) The use of positron emission tomography for early detection of recurrent head and neck squamous cell carcinoma in postradiotherapy patients. *Laryngoscope* **105(2):** 135–139.

Braams, J. W., Pruim, J., Freling, N. J., Nikkels, P. G., Roodenburg, J. L., Boering, G., Vaalburg, W., Vermey, A. (1995) Detection of lymph node metastases of squamous-cell cancer of the head and neck with FDG-PET and MRI. *Journal of Nuclear Medicine* **36(2):** 211–216.

Braams, J. W., Pruim, J., Kole, A. C., Nikkels, P. G., Vaalburg, W., Vermey, A., Roodenburg, J. L. (1997) Detection of unknown primary head and neck tumours by positron emission tomography. *International Journal of Oral Maxillofacial Surgery* **26(2):** 112–115.

Chaiken, L., Rege, S., Hoh, M. D., Choi, Y., Jabour, B., Juillard, G., Hawkins, R., Parker, R. (1993) Positron emission tomography with flurordeoxyclucose to evaluate tumour response and control after radiation therapy. *International Journal of Radiation Oncology Biology and Physics* **27:** 455–464.

DiChiro, G., DeLaPaz, R. L., Brooks, R. A. (1982) Glucose utilization of cerebral gliomas measured by (^{18}F) Fluorodeoxy glucose and positron emission tomography. *Neurology* **32:** 1323–1329.

Greven, M. K., Williams III, D. W., Keyes Jr. J. W., McGuirt, W. F., Watson, Jr. N. E., Randall, M. E., Raben, M., Geisinger K. R., Cappellari, J. O. (1994) Positron emission tomography of patients with head and neck carcinoma before and after high dose irradiation. *Cancer* **74:** 1355–1359.

Haberkorn, U., Strauss, L. G., Dimitrakopoulou, A., Seiffert, E., Oberdorfer, F., Ziegler, S., Reisser, C., Doll, J., Helus, F., van Kaick, G. (1993) Fluorodeoxyglucose imaging of advanced head and neck cancer after chemotherapy. *Journal of Nuclear Medicine* **34:** 12–17.

Hastings, D. L., Moore, J. V., Waller, M. L., Acton, P. D., Dodd, N. J., Hand, J. C., Nuttall, P. M., Jeavons, A. P. (1996) High resolution PET imaging of tumour using ^{18}FDG in *Quantitative Imaging in Oncology*. Proceedings of the 19th LH Gray Conference (Faulkner, K., Carey, B., Crellin, A. eds.) *British Journal of Radiology* London.

Laubenbacher, C., Saumweber, D., Wagner-Manslau, C., Kau, R. J., Herz, M., Avril, N., Siegler, S., Kruschke, C., Arnold, W., Schwaiger, M. (1995) Comparison of fluorine-18-fluorodoxyglucose PET, MRI and endoscopy for staging head and neck squamous-cell carcinomas. *Journal of Nuclear Medicine* **36(10):** 1747–1757.

Leskinnen-Kallio, S., Ruotsalainen, U., Nagren, K., Teras, M., Joensuu, H. (1991) Uptake of carbon-11-methionine and FDG in non Hodgkins lymphoma: a PET study. *Journal of Nuclear Medicine* **32:** 1211–1218.

McGuirt, W. F., Williams, III, D. W., Keyes, Jr. J. W., Greven, K. M., Watson, Jr. N. E., Geisinger, K. R., Cappellari, J. O. (1995) A comparative diagnostic study of head and neck nodal metastases using positron emission tomography. *Laryngoscope* **105(4 Pt 1):** 373–375.

Minn, H., Joensuu, H., Ahonen, A. (1988) Fluorodeoxyglucose imaging: a comparison with DNA flow cytometry in head and neck tumours. *Cancer* **61:** 1776–1781.

Moore, J. V., Hastings, D. L., Waller, M. L., Zhao, S., Acton, P. D., Jeavons, A. P., Dodd, N. J. F. (1998) Feasibility of imaging photodynamic injury to tumours by high resolution positron emission tomography: pre-clinical studies. *European Journal Nuclear Medicine* **25:** 1248–1254.

Mukherji, S. K., Drane, W. E., Mancuso, A. A., Parsons, J. T., Mendenhall, W. M., Stringer, S. (1996) Occult primary tumours of the head and neck: detection with 2-[F-18] fluoro-2-doxy-D-glucose SPECT. *Radiology* **199(3):** 761–766.

Price, P., Jones, T., on behalf of the EC PET Oncology Concerted Action and the EORTC PET Study Group (1995) Can positron emission tomography (PET) be used to detect subclinical response to cancer therapy? *European Journal of Cancer* **31A(12):** 1924–1927.

Rege, S., Maass, A., Chaiken, L., Hoh, C. K., Choi, Y., Lufkin, R., Anzai, Y., Juillard, G., Maddahi, J., Phelps, M. E. (1994) Use of positron emission tomography with fluorodeoxyglucose in patients with extracranial head and neck cancers. *Cancer* **73:** 3047–3058.

Siegel, S. (1956) *Non-Parametric Statistics for the Behavioural Sciences* Chapter 8. McGraw-Hill, New York, Toronto, London. pp 184–193.

Townsend, D. (1987) High density avalanche chamber (HIDAC) positron camera. *Journal of Nuclear Medicine* **28:** 1554–1562.

Wong, W. L., Chevretton, E. B., McGurk, M., Hussain, K., Davis, J., Beaney, R., Baddeley, H., Tierney, P., Maisey, M. (1997) A prospective study of PET-FDG imaging for the assessment of head and neck squamous cell carcinoma. *Clinical Otolaryngology* **22:** 209–214.

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