Editorial Review

Positron emission tomography – a useful imaging technique for otolaryngology, head and neck surgery?

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Positron emission tomography (PET) is a recent addition to the range of investigations available to the otolaryngologist. When used for tumour assessment, the technique depends on the differential uptake of tracer by different tissues. An intravenous injection of the radiotracer is given and, after an interval to allow tissue uptake to occur, the patient is placed in a scanner. As the radionuclide decays, positively charged particles (positrons) are released. These travel a short distance (1-2 mm) before combining with an electron resulting in two 511 KeV photons (annihilation radiation) which exit the tissues at approximately 180 degrees to each other. They are recorded by detectors in the scanner enabling a three-dimensional representation of events to be constructed (Wong et al., 1995).

The tracers are chosen to maximize the contrast between tumour uptake and normal tissues. Cancer cells have increased glycolysis and the radionuclide-labelled glucose analogue 2-[18F]fluoro-2-deoxyglucose-D-glucose (FDG) is most commonly used. Alternatives include L-[methyl-11C]methionine (Lindholm et al., 1993).

The majority of malignant tumours in the head and neck, excluding skin cancers, are mucosal squamous cell carcinomas with thyroid cancers being the second most common group. Clinical examination (including panendoscopy) combined with computed tomography (CT) and/or magnetic resonance image (MRI) scanning has a high sensitivity and specificity for detecting most primary head and neck cancers. PET scanning produces results which are approximately as good. When used for detecting nodal disease in the untreated neck, PET scanning performs marginally better than conventional investigations but still does not detect many occult nodal metastases (Rege et al., 1994; Braams et al., 1995; Wong et al., 1997). Reports of the use of PET for identifying occult primary cancers which present with nodal disease are scarce, but it is likely to successfully identify unknown primaries in between 25 and 66 per cent of cases (Rege et al., 1994; Wong et al., 1995).

Following treatment, the anatomical changes and scarring caused by surgery and radiotherapy often make it very difficult to assess whether recurrent or residual disease is present using clinical examination and conventional imaging techniques. PET scanning offers significant advantages as it depends on differential metabolic activity. In the majority of sites in the head and neck, PET has the ability to detect residual or recurrent disease at the primary site with a sensitivity of 88-100 per cent and specificity of 100 per cent compared to MRI and/or CT imaging sensitivity of 25-77 per cent and specificity of 75 to 80 per cent (Chaiken et al., 1993; Anzai et al., 1996; Wong et al., 1997). In the larynx PET scanning may be less sensitive than in other sites in the head and neck (Austin et al., 1995), but still has a high success rate in identifying disease following primary radiotherapy which may have been missed by conventional assessment (Rege et al., 1994; McGuirt et al., 1995).

In those cases where either chemotherapy or radiotherapy alone are used in the initial treatment phase, studies suggest that PET may have a useful role in monitoring the response to treatment. In those cases where the tumour uptake of isotope declines between pre- and post-treatment scans, the response to treatment is related to the extent of the decline. Where post-treatment uptake is similar to normal tissues, in some cases no detectable disease is found at subsequent operation (Chaiken et al., 1993; Greven et al., 1994a; Lindholm et al., 1995; Price and Jones, 1995). Following radiotherapy, repeat scanning at four months allows a better assessment of tumour status than if scanning is carried out at one month post-treatment (Greven et al., 1994b).

PET scanning is useful in the assessment of thyroid cancer. Whole body imaging relying on the affinity of the metastases to accumulate ¹³¹I or similar isotopes is usually performed. In less well differentiated thyroid cancers, ¹³¹I uptake may be poor or absent. This problem can be overcome by combining ¹³¹I and 18FDG-PET scans in the same patient. Some metastases are best demonstrated by PET, others by

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¹³¹I scanning, the difference largely being determined by the degree of differentiation within the tumour. When the two imaging techniques are combined, metastatic disease can be predicted with a sensitivity of 95 per cent (Feine *et al.*, 1996; Grunwald *et al.*, 1996). PET has also been found useful in the assessment of metastases in the less common medullary carcinoma of the thyroid (Simon *et al.*, 1996).

PET imaging may be used for investigating other head and neck tumours including paragangliomas and both benign and malignant salivary gland tumours. The role of PET in the evaluation of these tumours has yet to be fully determined. Studies using PET to differentiate benign from malignant salivary gland tumours have not shown any advantage over conventional imaging or fine needle aspiration cytology techniques (Keyes et al., 1994).

Recently the ability to co-register PET images with CT or MRI scans of the same patient has partially overcome the lack of precise anatomical detail which can be one of the problems of some PET images. This technique uses a computer algorithm to combine the PET and CT or MR images in one display using either anatomical landmarks or an automatic algorithm based on matching the pattern of signals from individual voxels. Co-registered PET images may be helpful in reducing overstaging of tumours using conventional techniques and can alter planned therapy. Disease which has been assessed as incurable may be found to be amenable to surgical resection (Wong et al., 1996).

PET has uses other than those related to tumour detection. PET scanning has proved to be an extremely useful tool in the quantitative determination of cerebral blood flow. This property, which makes PET a particularly useful tool for neurologists and psychiatrists, is sometimes useful in otolaryngology. Carotid artery resection may occasionally offer a chance of cure in patients with otherwise untreatable advanced head and neck carcinoma. Where interposition graft reconstruction is difficult, PET scanning coupled with temporary balloon occlusion enables the adequacy of the hemispheric collateral blood supply to be tested before carotid resection (Okamoto et al., 1996).

PET has some non-oncological uses for the otolaryngologist. It is proving a useful tool in the assessment of cochlear implants and their pattern of stimulation of the central nervous system. Studies using PET confirm clinical evidence that the primary auditory cortex does not develop normally in prelingually deaf subjects but that in post-lingually deaf subjects the primary auditory cortex may be reactivated by a cochlear implant after many years of deafness (Okazawa et al., 1996). Current studies have used adult subjects and thus data on the development of the primary auditory cortex in prelingually deaf children implanted at an early age is not available.

It is likely that as PET scanning and co-registration techniques are further refined, PET will be increasingly used in normal clinical practice. Areas where it is most likely to be of use in the head and neck include the assessment of recurrent tumours and post-treatment tumour surveillance.

References

- Anzai, Y., Carroll, W. R., Quint, D. J., Bradford, C. R., Monoshima, S., Wolf, G. T., Wahl, R. L. (1996) Recurrence of head and neck cancer after surgery or irradiation: prospective comparison of 2-deoxy-2-[F18]fluorodeoxyglucose PET and MR imaging diagnoses. *Radiology* 200: 135-141.
- Austin, J. R., Wong, F. C., Kim, E. E. (1995) Positron emission tomography in the detection of residual laryngeal carcinoma. Otolaryngology Head and Neck Surgery 113: 404-407
- 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 squamouscell cancer of the head and neck with FDG-PET and MRI. *Journal of Nuclear Medicine* 36: 211-216.
- Chaiken, L., Rege, S., Hoh, C., Choi, Y., Jabour, B., Juillard, G., Hawkins, R., Parker, R. (1993) Positron emission tomography with fluorodeoxyglucose to evaluate tumour response and control after radiation therapy. *International Journal of Radiation Oncology Biology Physics* 27: 455-464.
- Feine, U., Lietzenmayer, R., Hanke, J. P., Held, J., Wohrle, H., Muller-Schauenburg, W. (1996) Fluorine-18-FDG and Iodine-131-Iodide uptake in thyroid cancer. *Journal of Nuclear Medicine* 37: 1468-1472.
- Greven, K. M., Williams, D. W. 3rd., Keyes, J. W. Jr., McGuirt, W. F., Harkness, B. A., Watson, N. E. Jr., Raben, M., Frazier, L. C., Geisinger, K. R., Capellari, J. O. (1994a)
 Distinguishing tumour recurrence from irradiation sequelae with positron emission tomography in patients treated for larynx cancer. *International Journal of Radiation Oncology Biology Physics* 29: 841–845.
- Greven, K. M., Williams, D. W. 3rd, Keyes, J. W. Jr., McGuirt, W. F., Watson, N. E. Jr., Randall, M. E., Raben, M., Frazier, L. C., Geisinger, K. R., Capellari, J. O. (1994b) Positron emission tomography of patients with head and neck carcinoma before and after high dose irradiation. *Cancer* 74: 1355-1359.
- Grunwald, F., Schomburg, A., Bender, H., Klemm, E., Menzel, C., Bultmann, T., Palmedo, H., Ruhlmann, J., Kozac, B., Biersac, H. J. (1996) Fluorine-18 fluorodeoxyglucose positron emission tomography in the follow-up of differentiated thyroid cancer. *European Journal of Nuclear Medicine* 23: 312-319.
- Keyes, J. W. Jr., Harkness, B. A., Greven, K. M., Williams, D. W. 3rd., Watson, N. E. Jr., McGuirt, W. F. (1994) Salivary gland tumours: pretherapy evaluation with PET. *Radiology* 192: 99–102.
- Lindholm, P., Leskeninen-Kallio, S., Minn, H., Bergman, J., Haaparanta, M., Lehikoinen, P., Nagren, K., Ruotsalainen, U., Teras, M., Joensuu, H. (1993) Comparison of Fluorine-18-fluorodeoxyglucose and carbon-11-methionine in head and neck cancer. *Journal of Nuclear Medicine* 34: 1711-1716.
- Lindholm, P., Leskinen-Kallio, S., Grenman, R., Lehikoinen, P., Nagren, K., Teras, M., Ruotsalainen, U., Joensuu, H. (1995) Evaluation of response to radiotherapy in head and neck cancer by positron emission tomography and [11C] methionine. *International Journal of Radiation Oncology Biology Physics* 32: 787-794.
- McGuirt, W. F., Greven, K. M., Keyes, J. W. Jr., Williams, D. W. 3rd., Watson, N. E. Jr., Geisinger, K. R., Capellari, J. O. (1995) Positron emission tomography in the evaluation of laryngeal carcinoma. *Annals of Otology, Rhinology and Laryngology* 104: 274-278.
- Okamoto, Y., Inugami, A., Matzusaki, Z., Yokomizo, M., Konno, A., Togawa, K., Kuribayashi, R., Ogawa, T., Kanno, I. (1996) Carotid artery resection for head and neck cancer. *Surgery* **120:** 54-59.

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Okazawa, H., Naito, Y., Yonekura, Y., Sadato, N., Hirano, S., Nishizawa, S., Magata, Y., Ishizu, K., Tamaki, N., Honjo, I., Konishi, J. (1996) Cochlear implant efficiency in pre- and postlingually deaf subjects. A study with H2(15)O and PET. *Brain* 119: 1297–1306.

- Price, P., Jones, T. (1995) Can positron emission tomography (PET) be used to detect subclinical response to cancer therapy? The EC PET Oncology Concerted Action and the EORTC PET Study Group. European Journal of Cancer 31A: 1924–1927.
- Rege, S., Maass, A., Chaiken, L., Hoh, C. K., Choi, Y., Lufkin, R., Anzai, Y., Juillard, G., Maddahai, J., Phelps, M. E. (1994) Use of positron emission tomography with fluorodeoxyglucose in patients with extracranial head and neck cancers. *Cancer* 73: 3047–3058.
- Simon, G. H., Nitzsche, E. U., Laubenburger, J. J., Einart, A., Moser, E. (1996) PET imaging of recurrent medullary thyroid cancer. *Nuklearmedizin* 35: 102-104.
- Wong, W. L., Chevretton, E., McGurk, M., Croft, D. (1995) PET-FDG imaging in the clinical evaluation of head and neck cancer. *Journal of the Royal Society of Medicine* 88: 469-473.

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

carcinoma. Clinical Otolaryngology (in press).

Wong, W. L., Hussain, K., Chevretton, E., Hawkes, D. J., Baddeley, H., Maisey, M., McGurk, M. (1996) Validation and clinical application of computer-combined computed tomography and positron emission tomography with 2-[18] fluoro-2-deoxy-D-glucose head and neck images. American Journal of Surgery 172: 628-632.

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