SHORT COMMUNICATION

[11C]Methionine positron emission tomography for patients with persistent or recurrent hyperparathyroidism after surgery

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Abstract

Objective: Reoperation in patients with recurrent hyperparathyroidism usually requires localisation of abnormal glands. Current imaging techniques are not always successful in this group of patients. An evaluation of [11C]methionine positron emission tomography (PET) has been made to assess the ability of the technique to localise abnormal glands in patients with hyperparathyroidism after previous surgery.

Subjects and Methods: Eight patients (five with primary, and three with tertiary hyperparathyroidism) who had undergone one to three previous surgical explorations were studied. [11C]methionine PET scans of the neck and mediastinum were performed in all patients. All had recent technetium-99m (99mTc)-labelled sestamibi (n = 7) or thallium-201 (201Tl)/99mTc subtraction (n = 1) parathyroid scans available for comparison. Subsequent surgical correlation was available in all cases.

Results: [11C]methionine PET correctly located an abnormal site of uptake in all five patients with primary hyperparathyroidism compared with only one when conventional nuclear medicine methods were used. In the patients with tertiary hyperparathyroidism, [11C]methionine PET correctly located one, confirmed the absence of cervical or mediastinal abnormality in a patient with an autotransplanted forearm autonomous gland, and failed to demonstrate an abnormality in a third. 99mTc-labelled sestamibi scans were negative in all three patients.

Conclusion: [11C]methionine PET correctly locates abnormal parathyroid glands in the majority of patients with persistent or recurrent hyperparathyroidism after surgery in whom conventional non-invasive nuclear medicine imaging has failed.

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Introduction

At presentation of hyperparathyroidism many surgeons will operate without the use of preliminary imaging to locate the lesion. Indeed, Doppman suggested that the only localisation procedure required in these patients is to locate an experienced surgeon (1). The majority of patients are cured by means of this strategy, but a small percentage remain with persistent or recurrent hyperparathyroidism and some of them have ectopic glands (2). It is this group that require imaging before further, more technically difficult, surgical exploration. Anatomical cross-sectional and invasive imaging procedures exist, but have not shown superiority over the more widely used nuclear medicine procedures (1). A number of parathyroid glands will remain elusive, however, requiring further non-invasive or invasive imaging.

The use of [11C]methionine positron emission tomography (PET) in this context has been reported previously by one group (3, 4) who achieved high sensitivity, but in a mixed population of newly presenting and reoperative cases. We present our own early experience using this promising new technique solely in patients with persistent or recurrent hyperparathyroidism after previous surgery.

Patients and methods

We studied eight consecutive patients with recurrent hyperparathyroidism who had undergone one to three previous surgical explorations and had subsequent successful surgery. All had biochemical evidence of recurrent hyperparathyroidism [increased calcium (2.58–3.77 mmol/l, normal range 2.1–2.55 mmol/l) with inappropriate parathyroid hormone concentrations (29–2400 ng/l, normal range 10–65 ng/l)]. Five patients had primary and three had tertiary hyperparathyroidism. All patients had also had
technetium-99m (99mTc)-labelled sestamibi (n = 7) or thallium-201/technetium-99m (201Tl/99mTc) (n=1) parathyroid scintigraphic studies of the neck and mediastinum performed. Dual-phase 99mTc-labelled sestamibi scintigraphy was performed in four of the patients and subtraction scintigraphy with 99mTc was performed in the remaining 201Tl studies. None had tomographic studies performed.

PET studies were performed on a Siemens ECAT 951R PET scanner. Fifteen minutes after the intravenous injection of 370–740 MBq [11C]methionine, two contiguous 15-min emission scans were performed over the neck and then the upper mediastinum. This was followed by two 10-min transmission scans for correction of attenuation.

Results
Six of the eight patients showed abnormal focal accumulations of [11C]methionine in the neck (n = 2) (Fig. 1) or mediastinum (n = 4). Four of the five patients with primary hyperparathyroidism showed abnormalities that were subsequently surgically confirmed as adenomas. The fifth patient had a mediastinal gland, identified with PET, successfully ablated angiographically. Only one of these (a mediastinal adenoma) was located by sestamibi imaging. Of the three patients with tertiary hyperparathyroidism, one had an ectopic hyperplastic gland in the left carotid sheath correctly localised with PET. A second patient had a negative PET scan and a 0.25-g hyperplastic gland was subsequently excised from a normal position in the left lower neck. Sestamibi scans were negative in both these patients. A further patient who previously had had a forearm transplantation of parathyroid tissue was cured on removal of this tissue. Both PET and sestamibi scans of the neck and mediastinum correctly confirmed that there no residual abnormaly functioning parathyroid tissue elsewhere. The forearm was not scanned (Table 1).

Discussion
In our early experience, [11C]methionine PET has correctly localised abnormal parathyroid glands in most patients with recurrent hyperparathyroidism in whom conventional nuclear medicine techniques had been unsuccessful. Results for patients with primary hyperparathyroidism (five correct scans out of five) were better than those with tertiary disease (two of three scans correct), a difference commonly found with other localisation procedures (5). This use of [11C]methionine PET has previously been reported only by one group (3, 4) who achieved a sensitivity of between 80 and 85%, but in a mixed population of newly presenting and reoperative cases.

### Table 1 Results of investigation in eight patients with hyperparathyroidism.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Primary or tertiary disease</th>
<th>Serum Ca²⁺†</th>
<th>Serum PTH</th>
<th>PET result</th>
<th>Sestamibi/Tl result</th>
<th>No. of previous operations</th>
<th>Gland weight (g)</th>
<th>Histology</th>
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<tr>
<td>A</td>
<td>58</td>
<td>F</td>
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<td>3.77</td>
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<td>+m</td>
<td>+m</td>
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<tr>
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<td>1</td>
<td>2.76</td>
<td>112</td>
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<td>N/A‡</td>
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<tr>
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<td>62</td>
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<td>2.92</td>
<td>144</td>
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<td>–</td>
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<td>2</td>
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<tr>
<td>D</td>
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<td>341</td>
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<td>0.66</td>
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<td>E</td>
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<td>1</td>
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<td>54</td>
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</tr>
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<td>F</td>
<td>3</td>
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<td>–*</td>
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<td>N/A</td>
</tr>
<tr>
<td>H</td>
<td>46</td>
<td>F</td>
<td>3</td>
<td>2.76</td>
<td>29</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>0.25</td>
<td>Hyperplasia</td>
</tr>
</tbody>
</table>

†Serum calcium (corrected).
‡Angiographic embolisation.
*Autonomous transplanted forearm gland, true negative PET and 99mTc-labelled sestamibi scans.
PTH, parathyroid hormone; c, cervical; m, mediastinal; cs, carotid sheath; +, positive; –, negative N/A, not applicable.
PET offers advantages over single photon imaging, including greater spatial resolution, the incorporation of tomography as a routine, and the use of labelled, naturally occurring substances that are more likely than analogues to behave physiologically.

Many alternative invasive and non-invasive techniques exist for parathyroid localisation. None have shown clear superiority; however, and scintigraphic techniques are likely to remain the ones of first choice, particularly since the introduction of $^{99m}$Tc-labelled sestamibi. In this series, there was a much greater sensitivity for localisation of abnormal parathyroid glands than with $^{99m}$Tc-labelled sestamibi and $^{201}$TI/$^{99m}$Tc imaging. This is likely to be explained in part by a selection bias, as many of the patients were referred after negative conventional nuclear medicine scintigraphy and so were preselected as being scintigraphy-negative. A further study comparing $^{[11C]}$methionine PET with $^{99m}$Tc-labelled sestamibi with tomography before any imaging would be a more equitable direct comparison of the two techniques.

The conclusion from this study, in view of this point, the scarcity of clinical PET centres, and the cost of the procedure, is that $^{[11C]}$methionine PET does not have a role in routine imaging for hyperparathyroidism and should be reserved for patients who have undergone previous surgery and in whom other radionuclide imaging has failed, or in whom anatomical imaging techniques had shown a structural abnormality, the nature of which requires confirmatory functional evaluation before reoperation. The number of patients falling into these categories is likely to be relatively small compared with the number of patients requiring surgery for hyperparathyroidism, but these early results with $^{[11C]}$methionine PET suggest that this technique may offer a non-invasive answer for this problematic group.

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References

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