Clinical Research Paper

Role of $^{18}$F-FDG PET/CT in diagnosis and staging of nasopharyngeal carcinoma

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Key words: nasopharyngeal carcinoma, TNM staging, $^{18}$F-FDG PET/CT, MRI

Background and Objective: Because $^{18}$F-FDG PET/CT can display cancer lesion's morphology, size and the relationship of the cancer lesion to adjacent tissues, it is used in the diagnosis and classification of nasopharyngeal carcinoma (NPC). This study was to explore the application value of $^{18}$F-FDG PET/CT in TNM staging by comparing the performance of MRI and PET/CT together with pathological results for some small lymph nodes. Methods: Sixty-eight pathologically proven NPC patients were selected from September 2005 to March 2007 in Sun Yat-sen University Cancer Center. All cases underwent both MRI and $^{18}$F-FDG PET/CT examinations. PET two-dimensional (2D) data were collected. Automatic dose tracking scanning and contrast-enhanced CT scanning were performed. $^{18}$F-FDG was intravenously administrated at a dose of 3.7–5.5 MBq/kg. MRI T1W, T2W and T1W Gd-DTPA enhanced images were obtained. Neck lymph nodes of ten NPC patients were pathologically examined. Results: Nasopharyngeal carcinoma lesions of 68 cases were all clearly displayed by both PET/CT and MRI. Among 138 small lymph nodes smaller than 1 cm in diameter which were positively detected by PET/CT, only 28.0% were suggested questionable by MRI scanning. Fourteen out of sixteen (87.5%) positive lymph nodes detected by PET/CT from 10 patients were pathologically confirmed. Both PET/CT and MRI revealed enlarged lymph nodes of the neck. Some lymph nodes whose proliferation was inhibited during radiotherapy suggested by PET/CT were displayed intensified images by contrast-enhanced PET/CT and MRI. Metastases to lung, bone and liver in eight stage IVb patients were clearly displayed by PET/CT, but not by MRI. The stage of 23 patients was adjusted after PET/CT imaging. Conclusion: $^{18}$F-FDG PET/CT with automatic dose tracking scanning protocol and contrast-enhanced scanning can provide more comprehensive information than MRI in diagnosing and staging of NPC.

The tumor TNM staging of nasopharyngeal carcinoma (NPC) is the determine factor in choosing the proper treatment protocol. Magnetic resonance imaging (MRI) and computed tomography (CT) scans are the conventional tools to classify the stage of NPC patients. Due to the high resolution and high sensitivity of MRI in detecting soft tissues, MRI can clearly display the NPC tumor foci. MRI, however, cannot show the proliferation of cancer cell. It is also difficult for MRI to identify tissue fibrosis caused by radiotherapy, early metastasis, and recurrence, especially in lymph nodes whose diameters are less than 1 cm. PET/CT, which adopts automatic dose tracking, significantly increases the resolution for detecting tissues, displays the tumor morphology and surrounding tissues precisely, thereby to reveal the clone distribution of cancer cells at different proliferative stages and distant metastatic lesions. By comparing with pathology of some small lymph nodes, this study adopted whole body scans using $^{18}$-fluoro-2-deoxyglucose (FDG) PET/CT and head and neck scans using MRI to explore the application of $^{18}$F-FDG PET/CT in TNM staging in 68 NPC patients.

Material and Methods

Imaging instruments and reagents. GE Discovery ST 16 PET/CT scanner and GE CVi 1.5T MRI scanner were used. $^{18}$F-FDG, with the radiopurity of more than 95%, was purchased from Beijing Atom HighTech Co., Ltd.

Patients. From September 2005 to March 2007, 68 pathologically diagnosed NPC patients in Sun Yat-sen University Cancer Center were selected randomly to undergo PET/CT and MRI scan. There were 40 males and 28 females (age 24–56 years, with a mean age of 41 years); and six cases were grade II and 62 were grade III according to WHO standard. $^{18}$F-FDG PET/CT scanning was performed as follows: 2D data collecting model was used to collect PET data; and automatic dose tracking was used for CT scanning (volt: 140 kV, current: 140–230 mA). Enhanced angiography was performed in some patients. Scanning was started at 50 min after intravenous injection of 3.7–5.5 MBq/kg $^{18}$F-FDG and the collecting time lasted 2.5–3 min/
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### Table 1  Comparisons of lymph nodes of the neck between PET/CT and MRI in 68 NPC patients

<table>
<thead>
<tr>
<th></th>
<th>Lymph nodes ≥ 1 cm (cases)</th>
<th>Lymph nodes &lt; 1 cm (cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET/CT</td>
<td>MRI positive</td>
<td>MRI negative</td>
</tr>
<tr>
<td>Positive</td>
<td>102</td>
<td>0</td>
</tr>
<tr>
<td>Negative</td>
<td>15</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 2  Comparisons of T staging and N staging of 68 patients with NPC based on MRI images

<table>
<thead>
<tr>
<th>T staging</th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>T2</td>
<td>2</td>
<td>17</td>
<td>1</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>T3</td>
<td>0</td>
<td>26</td>
<td>10</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>T4</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>43</td>
<td>13</td>
<td>8</td>
<td>68</td>
</tr>
</tbody>
</table>

### Table 3  Comparisons of the stage between PET/CT and MRI in 68 patients with NPC

<table>
<thead>
<tr>
<th>Staging</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IVa</th>
<th>IVb</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET/CT</td>
<td>3</td>
<td>12</td>
<td>32</td>
<td>11</td>
<td>10</td>
<td>68</td>
</tr>
<tr>
<td>MRI</td>
<td>2</td>
<td>19</td>
<td>37</td>
<td>8</td>
<td>2</td>
<td>68</td>
</tr>
<tr>
<td>Adjustment</td>
<td>1</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>8</td>
<td>24</td>
</tr>
</tbody>
</table>

Twelve out of 68 NPC patients underwent $^{18}$F-FDG PET/CT and MRI before, during and after radiotherapy (20–30Gy). The $^{18}$F-FDG metabolism was found high in NPC lesions of these 12 patients before radiotherapy; and MRI scan also revealed the same nasopharyngeal lesions. The $^{18}$F-FDG metabolism remained high in nasopharyngeal lesions of two patients during radiotherapy, which were also exhibited by MRI scan. After radiotherapy, PET/CT showed that the nasopharyngeal lesions of all patients shrank, $^{18}$F-FDG metabolism became inactive, and uneven enhancements were observed; while MRI found the existence of nasopharyngeal lesions in four patients.

Comparison of $^{18}$F-FDG PET/CT and MRI in regional nasopharyngeal lymph nodes of NPC patients. Both $^{18}$F-FDG PET/CT and MRI identified the swollen lymph nodes whose diameters were ≥ 1 cm. Positive lymph nodes revealed high $^{18}$F-FDG metabolism, while negative lymph nodes showed normal or low $^{18}$F-FDG metabolism.

Thirty-nine out of 138 positive lymph nodes whose diameters were ≤ 1 cm and identified by PET/CT, were not assured of positive lymph nodes by MRI, accounting for 28.0% (39/138) (Table 1). Ten patients underwent biopsy on their neck lymph nodes. Fourteen out of 16 positive lymph nodes detected by PET/CT were confirmed by pathological examination; while MRI was not certain about eight lymph nodes and found the other eight lymph nodes negative.

Comparison of $^{18}$F-FDG PET/CT and MRI in NPC staging. Sixty-eight NPC patients were staged according to the criteria proposed on the Fuzhou Convention in 1992, mainly based on CT images. Recently, MRI has become the prevalent diagnostic tool, and the image diagnosis for NPC has gradually shifted to MRI. Some researchers even suggest classifying NPC based on MRI scanning results.1

Comparison of $^{18}$F-FDG PET/CT and MRI in NPC staging. Sixty-eight NPC patients were staged according to the criteria of '92 staging system for NPC based on MRI results. $^{18}$F-FDG PET/CT showed that distant metastases to lung, bone, and liver occurred in eight patients, and there was no obvious $^{18}$F-FDG metabolism in some lung lesions. However, these metastases were not detected by MRI due to its limitation in the scanning scope. Metastasis to small supraclavicular lymph nodes was found in two patients. The stage of 22 NPC patients was adjusted after $^{18}$F-FDG PET/CT scan, among which the stage of 10 patients was adjusted higher and that of 12 patients was adjusted lower, with a total adjustment rate of 34.0% (Tables 2 and 3).

### Discussion

The staging for NPC adopts the criteria proposed on the Fuzhou Convention in 1992, mainly based on CT images. Recently, MRI has become the prevalent diagnostic tool, and the image diagnosis for NPC has gradually shifted to MRI. Some researchers even suggest classifying NPC based on MRI scanning results.1 $^{18}$F-FDG PET/CT scan is an effective method for tumor diagnosis, staging and therapy evaluation.4 The distribution and proliferation of cancer cells inside the lesions and the tumor burden influence the T staging of the tumor. The N staging based on the size of the lymph node can not completely reflect lymph node metastasis.
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Some researches reveal that PET/CT is superior to either PET or CT with respect to tumor staging. Moreover, compared with the single low dose PET/CT, the high dose PET/CT with enhancement of angio-scan is even more efficient, which can increase the diagnostic rate by 8.0% in head-neck cancer and lung cancer. Some researchers even consider PET/CT with enhancement of angio-scan to be indispensable to 3-D radiotherapy and non-regular operation.

Hu et al. suggest 18F-FDG PET/CT is better than MRI in evaluating lymph node metastasis. Other scholars also propose that the number of positive lymph nodes identified by PET/CT, CT, and MRI are different. MRI can identify more positive lymph nodes than PET/CT, but there is no difference between CT and MRI. In addition, the gross tumor volume (GTV) of radiotherapeutic target region confirmed by 18F-FDG PET/CT is often smaller than that confirmed by MRI.

18F-FDG is the proper radiopharmaceutical for detecting NPC, which is originated from squamous epithelium with abnormal glycometabolism. Sixty out of 68 NPC patients in this study were found positive both by MRI and PET/CT. Lesions displayed high metabolism, and MRI showed medium intensity in the lump. Five out of 68 NPC patients were negative both in PET/CT and MRI. This might be because that cancer cells were too few to be identified by the scanner. PET/CT and MRI results were consistent in 65 out of 68 NPC patients, yielding an identical rate of 95.5%. Three cases which were negative in MRI were found abnormally active 18F-FDG metabolism by PET/CT. Due to the dispersion of high energy photons, the lesion borderlines scanned by PET/CT were not sharp enough to delineate the radiotherapeutic target region. This problem may be solved by adding an enhancement scan.

It is reported that 18F-FDG PET/CT is superior to MRI and CT in evaluating the neck lymph node metastasis in NPC. The sensitivity and specificity of 18F-FDG PET/CT were 90.0% and 94.0%, respectively; while those of CT were 82.0% and 85.0% and those of MRI were 80.0% and 79.0%. Recently, some researchers report that the identification rate of PET/CT, MRI, and CT on retropharyngeal lymph nodes of 53 patients were 37.0%, 67.0%, and 58.0%, respectively. The positive rate of 18F-FDG PET/CT was notably lower than that of MRI and CT, which might result from the low scanning voltage and inefficient resolution of tissues.

It is shown in this study that both MRI and PET/CT clearly displayed the neck lymph nodes of NPC patients whose shorter diameters were ≥ 1 cm with active metabolism equally well. MRI and CT could also detect positive neck lymph nodes whose diameter were ≤ 1 cm with normal or low metabolism of 18F-FDG. In the detection rate of PET/CT was significantly higher than that of MRI in detecting pathologically confirmed lymph nodes less than 1 cm in the short diameter, indicating that 18F-FDG metabolism is more specific and sensitive in diagnosing lymph node metastasis than morphological changes of NPC. We found that in comparison to pathological examination, PET/CT performed on the neck lymph nodes in 10 NPC patients yielded a positive rate of as high as 87.5%, which was higher than studies reported above. This difference might result from the CT dose tracking scan and the CT enhancement scan we used to improve tissue resolution.

In addition to displaying regional lesions, regional lymph nodes, and metastasis to other organs in the same region, 18F-FDG PET/CT could also easily find other distant metastasis based on the whole body scan. Among the 68 NPC patients, we found metastasis to lung, bone, and liver in eight patients with the help of PET/CT. The N stage of two NPC patients was adjusted because metastases to supraclavicular lymph nodes were found by 18F-FDG PET/CT; and the stage of 23 NPC patients were also adjusted after PET/CT scan.

Figure 1. Enhanced CT (A), MRI (B) and PET/CT (C) images of small lymph node of the left neck. The black arrow in (C) shows the fused PET/CT image of metastatic lymph node of the left neck, 7mm in diameter, with high uptake.

Figure 2. MRI (A) and PET/CT (B)images of the left retropharyngeal lymph node. The black arrow in (B) shows the fused image of the left retropharyngeal metastatic lymph node proven by pathological examination with high uptake.
Twelve NPC patients underwent PET/CT and MRI examinations again during regional radiotherapy at a dose of 20–30 Gy. Original lesions and parts of metastatic lymph nodes were gradually dwindled and cellular glycometabolism almost returned to the normal level; and uneven intensity in lesions was presented by CT and MRI enhancement scan. These indicate that radiotherapy has great effect on the metabolism of $^{18}$F-FDG of cancer cells, and suppressed cellular metabolism would result in decreased metabolism of $^{18}$F-FDG. $^{18}$F-FDG metabolism is more sensitive in reflecting the changes in tissue structures than CT and MRI. As for small metastatic lesions in the lung ($\leq 1$ cm), $^{18}$F-FDG metabolism had no obvious changes because of considerably fewer cancer cells. Therefore, careful consideration should be made on the status of the disease, treatment regimens and structure changes in the lesion to classify the clinical stage of NPC.

In conclusion, combined with disease history, $^{18}$F-FDG PET/CT with automatic dose tracking scanning protocol and contrast-enhanced scanning could provide more comprehensive information than MRI in diagnosing and staging NPC.

References


