

# Combined Positron Emission Tomography and Computed Tomography

## Option or necessity?

Naima K. Al-Bulushi

التصوير المقطعي بالإصدار البوزيتروني المصاحب للتصوير المقطعي المحوسب  
خيار أم ضرورة؟

نعيمة خميس البلوشية

**I**N THIS ISSUE OF SQUMJ, JAFFERBHOY *et al.* have shared their regional experience about the impact of adding positron emission tomography (PET)/computed tomography (CT) to conventional CT in the preoperative work-up and follow-up of a select group of patients with colorectal cancer.<sup>1</sup> In their retrospective study, PET/CT had a major impact in the preoperative and follow-up groups, altering the management of 73% and 64% of cases, respectively. According to the authors, they selected colorectal cancer as the focus of their investigation as it is one of the most common cancers in the UK;<sup>1</sup> indeed, the survival rates of breast, colorectal and cervical cancer have more than doubled in the last six decades.<sup>2</sup> The situation is similar in Oman, with colon cancer among the top 10 most common cancers for both genders.<sup>3</sup> Therefore, the utilisation of PET/CT for colorectal cancer patients in Oman may also lead to a change in management for the majority of these patients.

In colorectal cancer, surgery is the potential curative treatment for localised disease in addition to chemoradiotherapy in selected cases. Salvage surgeries are usually performed for patients with recurrent disease and metastasectomies are an option for distant metastasis in some patients. In Oman, there is a lack of national screening programmes for common cancers such as breast, colorectal and prostate cancers; this may result in the late presentation of some cases. As such, it is very important to establish accurate preoperative staging of the disease. Furthermore, close monitoring and regular follow-up is essential in the postoperative period, as more than 85% of distant metastasis cases will appear within the first three years and all cases of metastasis in the first five years.<sup>4</sup> Identifying cases of disease recurrence and managing them as early as

possible improves the overall survival rate—it is at this point that PET/CT can play a significant role.<sup>3</sup> PET/CT can not only aid in the early detection of recurrence but can also accurately determine recurrence when CT alone cannot identify the lesion, as shown by Jafferbhoy *et al.*<sup>1</sup>

In their study, Jafferbhoy *et al.* used <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG)-PET/CT to evaluate patients preoperatively and during follow-up in order to detect early recurrence;<sup>1</sup> this method is also recommended in the literature.<sup>5,6</sup> The main indication for using PET/CT in this cohort was either as a problem-solving measure, in cases where conventional CT was equivocal or patients had rising carcinogenic embryonic antigen levels with negative CT results, or as a confirmatory tool, for patients who had resectable metastatic disease or evidence of disease recurrence on conventional CT. In the latter group, PET/CT was used to confirm the CT findings prior to surgery.<sup>1</sup> In Oman, other state-of-the-art modalities are used in the staging and follow-up of oncological patients, including 64-slice CT and 3Tesla magnetic resonance imaging machines, as well as trained and well-equipped surgical teams. Nevertheless, PET/CT can be a major contributor and aid in more effective utilisation of this expensive equipment and accompanying human resources. This technology will confirm findings in some cases as well as potentially identify recurrent disease that may be missed by other modalities.

In an extensive review of all published randomised clinical trials and systematic reviews, Fletcher *et al.* proposed a number of recommendations for the utilisation of PET/CT in oncological patients.<sup>6</sup> Primarily, the authors recommended that <sup>18</sup>F-FDG-PET/CT be used for the diagnosis of lung, pancreas and head and neck cancers as well as cancers of unknown

primary. In addition,  $^{18}\text{F}$ -FDG-PET/CT should be utilised for staging breast, colon, oesophageal, lung, head and neck lymphomas and melanomas. Fletcher *et al.* also advocated that this modality be used for detecting the recurrence of colorectal, breast, head, neck and thyroid cancers and lymphomas.<sup>6</sup> Apart from using PET/CT in staging, restaging and the evaluation of distant metastatic disease and local recurrence, it has a very important role in monitoring treatment. Traditionally, PET/CT has been used to assess the treatment response at the end of chemotherapy cycles as well as the overall response at the end of therapy.<sup>7</sup> However, more recent literature has shown that evaluating the response mid-treatment is useful to assess the response to that particular regime, as the waiting until the end of treatment to determine the patient's response might be too late in some cases.<sup>8,9</sup> To this end, combined PET/CT can help in ensuring the cost-effective utilisation of expensive chemotherapy treatments.

In their retrospective analysis of the cost-effectiveness of mid-treatment PET/CT, Moulin-Romsee *et al.* reported that performing PET/CT after three chemotherapy cycles in patients with non-Hodgkin's lymphoma saved an average of €1,879 per patient.<sup>10</sup> Oman may potentially be an even better beneficiary than some European countries. Until a specific tumour-targeted therapy is readily available for oncologists and cancer patients in this country, PET/CT is the best option. Further research has confirmed its efficiency in evaluating the early response to treatment—one such study noted that it could be used even as early as a week after a cycle of chemotherapy.<sup>11</sup>

FDG-PET/CT is invaluable for more than just the above-described oncological indications. An interesting emerging application of FDG-PET is for thrombus imaging; this was initially discovered incidentally in aneurysms with *thrombi*.<sup>12</sup> Another novel and fascinating aspect of FDG-PET/CT was discovered by Figueroa *et al.*; the imaging modality did not just predict the occurrence of cardiovascular disease (CVD) but also the potential timeframe of CVD events.<sup>13</sup> In Oman, the incidence of CVD is the highest among all communicable and non-communicable diseases, with the proportional mortality due to CVD at 33%.<sup>14</sup> In comparison, proportional mortality due to either diabetes or cancer were 10% each.<sup>14</sup> Thus, introducing this modality in Oman will certainly have a considerable supplemental benefit to the health and welfare of Omani citizens—not only in the oncological context, but also in terms of the early detection of cardiac events and the reduction of cardiovascular-related mortality.

Nonetheless, it is important to consider a few

limitations to PET/CT imaging. As mentioned by Ben-Haim *et al.*, high blood glucose reduces the overall quality of PET/CT images.<sup>2</sup> Abnormal lesions may therefore be missed in diabetics without controlled glucose levels. However, this problem may be overcome by using other non-FDG-PET/CT radiotracers (e.g. choline or methionine) which are not affected by high blood glucose levels. The other limitation of FDG-PET/CT is the increased uptake of the tracer in cases of infection which can mimic that of tumours. While this can be considered a disadvantage of the modality, this feature of FDG-PET/CT has actually been utilised to image and evaluate patients with osteomyelitis, sarcoidosis and inflammatory bowel disease, where it showed high sensitivity in detecting the site of the lesions.<sup>15</sup> It was also used for imaging purposes in patients with fever of unknown origin; due to the high affinity of FDG uptake at the sites of infection and inflammation, the modality was found to have a high sensitivity in detecting abnormalities.<sup>16</sup>

An additional limitation to the PET/CT modality, one which is probably unique to Oman, is its current non-availability within the country. Currently, only a small group of patients selected by a number of committees are able to benefit from PET/CT imaging abroad. So far it has been used as a problem-solving modality in cases where both other imaging modalities and tissue biopsies have proved inconclusive. Data analysis has clearly shown that the number of cancer patients in Oman is increasing, as it is globally.<sup>17</sup> Thousands of potential patients would benefit from this service if it was made available in-house. The fact that patients have to be sent abroad for PET/CT scans creates many logistic impediments as well as significantly underutilising one of the most effective and state-of-the-art modalities for oncological patients—not to mention the fact that it is uneconomical to send patients abroad to receive this service.<sup>17</sup>

One of the fundamental human rights is the right to health. This necessarily involves the creation of a well-governed, financially secure, responsive and innovative health system that delivers services freely according to need.<sup>18</sup> Unsurprisingly, we are currently facing an increase in the global incidence of cancer. According to the worldwide GLOBOCAN project, there were 14.1 million new cancer cases and 8.2 million deaths due to cancer in 2012.<sup>19</sup> Those numbers are expected to increase, with 22.2 million new cancer cases predicted for 2030.<sup>20</sup> With such an immense surge in cancer patients expected within the next few decades, health services will face the significant challenge of coping with healthcare-related expenses. The optimisation and cost-effective utilisation of

available resources would be the most effective method to ensure the burden is not too great. This is particularly true for countries where healthcare is provided free to citizens by the government, such as in Oman. When it comes to managing oncological patients, PET/CT has proven without a doubt to be the leading modality. Over the last four decades, Oman has borne witness to vast improvements in health services with health providers continuing to pursue excellence; however, this excellence cannot be achieved without the establishment of a national PET/CT service in Oman.

## References

- Jafferbhoy S, Chambers A, Mander J, Paterson H. Selective use of 18F-fluorodeoxyglucose-positron emission tomography and computed tomography in the management of metastatic disease from colorectal cancer: Results from a regional centre. *Sultan Qaboos Univ Med J* 2015; 15:52–57.
- Ben-Haim S, Ell P. 18F-FDG PET and PET/CT in the evaluation of cancer treatment response. *J Nucl Med* 2009; 50:88–99. doi: 10.2967/jnumed.108.054205.
- Ministry of Health Oman, Oman National Cancer Registry. Cancer Incidence in Oman: Report of 2010. Muscat, Oman: Ministry of Health, 2010.
- Casciato DA. *Manual of Clinical Oncology*. 5th ed. Philadelphia, Pennsylvania, USA: Lippincott Williams & Wilkins, 2004. P. 207.
- Herbertson RA, Scarsbrook AF, Lee ST, Tebbutt N, Scott AM. Established, emerging and future roles of PET/CT in the management of colorectal cancer. *Clin Radiol* 2009; 64:225–37. doi: 10.1016/j.crad.2008.08.008.
- Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, et al. Recommendations on the use of 18F-FDG PET in oncology. *J Nucl Med* 2008; 49:480–508. doi: 10.2967/jnumed.107.047787.
- Ueda S, Saeki T. Early prediction of tumor response: A future strategy for optimizing cancer treatment. In: Misciagna S, Ed. *Positron Emission Tomography: Recent developments in instrumentation, research and clinical oncological practice*. Rijeka, Croatia: InTech Open Access Co., 2013. Pp. 257–74.
- Skougaard K, Nielsen D, Jensen B, Hendel H. Comparison of EORTC criteria and PERCIST for PET/CT response evaluation of patients with metastatic colorectal cancer treated with irinotecan and cetuximab. *J Nucl Med* 2013; 54:1026–31. doi: 10.2967/jnumed.112.111757.
- Khong PL, Huang B, Phin Lee EY, Sum Chan W, Kwong YL. Mid-treatment 18F-FDG PET/CT scan for early response assessment of SMILE therapy in natural killer/T-cell lymphoma: A prospective study from a single center. *J Nucl Med* 2014; 55:911–16. doi: 10.2967/jnumed.113.131946.
- Moulin-Romsee G, Spaepen K, Stroobants S, Mortelmans L. Non-Hodgkin lymphoma: Retrospective study on the cost-effectiveness of early treatment response assessment by FDG-PET. *Eur J Nucl Med Mol Imaging* 2008; 35:1074–80. doi: 10.1007/s00259-007-0690-0.
- Guo J, Guo N, Lang L, Kiesewetter D, Xie Q, Li Q, et al. (18)F-alfatide II and (18)F-FDG dual-tracer dynamic PET for parametric, early prediction of tumor response to therapy. *J Nucl Med* 2014; 55:154–60. doi: 10.2967/jnumed.113.122069.
- Muzaffar R, Kudva G, Nguyen NC, Osman MM. Incidental diagnosis of thrombus within an aneurysm on 18F-FDG PET/CT: Frequency in 926 patients. *J Nucl Med* 2011; 52:1408–11. doi: 10.2967/jnumed.111.091264.
- Figuerola AL, Abdelbaky A, Truong QA, Corsini E, MacNabb MH, Lavender ZR, et al. Measurement of arterial activity on routine FDG PET/CT images improves prediction of risk of future CV events. *JACC Cardiovasc Imaging* 2013; 6:1250–9. doi: 10.1016/j.jcmg.2013.08.006.
- World Health Organization. *Noncommunicable Diseases (NCD) Country Profiles, 2014: Oman*. From: [www.who.int/nmh/countries/omn\\_en.pdf?ua=1](http://www.who.int/nmh/countries/omn_en.pdf?ua=1) Accessed: Oct 2014.
- Gotthardt M, Bleeker-Rovers CP, Boerman OC, Oyen WJ. Imaging of inflammation by PET, conventional scintigraphy, and other imaging techniques. *J Nucl Med* 2010; 51:1937–49. doi: 10.2967/jnumed.110.076232.
- Keidar Z, Gurman-Balbir A, Gaitini D, Israel O. Fever of unknown origin: The role of 18F-FDG PET/CT. *J Nucl Med* 2008; 49:1980–5. doi: 10.2967/jnumed.108.054692.
- Al-Bulushi NK, Bailey D, Mariani G. The medical case for a positron emission tomography and X-ray computed tomography combined service in Oman. *Sultan Qaboos Univ Med J* 2013; 13:491–501.
- Horton R. What does a National Health Service mean in the 21st century? *Lancet* 2008; 371:2213–18. doi: 10.1016/S0140-6736(08)60956-3.
- International Agency for Research on Cancer and World Health Organization. *GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012 - All Cancers (excluding non-melanoma skin cancer)*. From: [globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx) Accessed: Oct 2014.
- Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): A population-based study. *Lancet Oncol* 2012; 13:790–801. doi: 10.1016/S1470-2045(12)70211-5.